

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	14	(amyloid near4 peptide) same (diameter or aggregate)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L2	4	l1 same length	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L3	91	(amyloid near4 peptide) and (diameter same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L4	36	l3 and glutamine	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:50

BIOTECHNO' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

CONFSCI' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 Cambridge Scientific Abstracts (CSA)

HEALSAFE' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 Cambridge Scientific Abstracts (CSA)

IMSDRUGCONF' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 IMSWORLD Publications Ltd.

LIFESCI' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 Cambridge Scientific Abstracts (CSA)

MEDICONF' ENTERED AT 15:19:39 ON 16 DEC 2004
GHT (C) 2004 FAIRBASE Datenbank GmbH, Hannover, Germany

PASCAL' ENTERED AT 15:19:39 ON 16 DEC 2004
production or dissemination in part or in full,
ns of any process and on any support whatsoever
hibited without the prior written agreement of INIST-CNRS.
GHT (C) 2004 INIST-CNRS. All rights reserved.

g repeat) and aggregate and length and diameter
0 FILE AGRICOLA
0 FILE BIOTECHNO
0 FILE CONFSCI
0 FILE HEALSAFE
0 FILE IMSDRUGCONF
0 FILE LIFESCI
0 FILE MEDICONF
0 FILE PASCAL

FOR ALL FILES
0 (CAG REPEAT) AND AGGREGATE AND LENGTH AND DIAMETER

e .chemistry
N U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
ESTIMATED COST 6.83 7.25

CAPLUS' ENTERED AT 15:20:24 ON 16 DEC 2004
SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
SEE "HELP USAGETERMS" FOR DETAILS.
GHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

BIOTECHNO' ENTERED AT 15:20:24 ON 16 DEC 2004
GHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

COMPENDEX' ENTERED AT 15:20:24 ON 16 DEC 2004
Index Compilation and Indexing (C) 2004
er Engineering Information Inc (EEI). All rights reserved.
Index (R) is a registered Trademark of Elsevier Engineering Information Inc.

ANABSTR' ENTERED AT 15:20:24 ON 16 DEC 2004
GHT (C) 2004 THE ROYAL SOCIETY OF CHEMISTRY (RSC)

CERAB' ENTERED AT 15:20:24 ON 16 DEC 2004
GHT (C) 2004 Cambridge Scientific Abstracts (CSA)

METADEX' ENTERED AT 15:20:24 ON 16 DEC 2004

COPYRIGHT (c) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'USPATFULL' ENTERED AT 15:20:24 ON 16 DEC 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> (cag repeat) and aggregate and length and diameter

L10	0	FILE CAPLUS
L11	0	FILE BIOTECHNO
L12	0	FILE COMPENDEX
L13	0	FILE ANABSTR
L14	0	FILE CERAB
L15	0	FILE METADEX
L16	0	FILE USPATFULL

TOTAL FOR ALL FILES

L17	0	(CAG REPEAT) AND AGGREGATE AND LENGTH AND DIAMETER
-----	---	--

=> glutamine and aggregate and length and diameter

L18	0	FILE CAPLUS
L19	0	FILE BIOTECHNO
L20	0	FILE COMPENDEX
L21	0	FILE ANABSTR
L22	0	FILE CERAB
L23	0	FILE METADEX
L24	1	FILE USPATFULL

TOTAL FOR ALL FILES

L25	1	GLUTAMINE AND AGGREGATE AND LENGTH AND DIAMETER
-----	---	---

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregate or assembly) and length

L26	2	FILE CAPLUS
L27	1	FILE BIOTECHNO
L28	0	FILE COMPENDEX
L29	0	FILE ANABSTR
L30	0	FILE CERAB
L31	0	FILE METADEX
L32	50	FILE USPATFULL

TOTAL FOR ALL FILES

L33	53	(CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH
-----	----	---

=> dup rem

ENTER L# LIST OR (END):126-127

PROCESSING COMPLETED FOR L26

PROCESSING COMPLETED FOR L27

L34	3	DUP REM L26-L27 (0 DUPLICATES REMOVED)
-----	---	--

=> d l34 ibib abs total

L34 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:716876 CAPLUS

DOCUMENT NUMBER: 139:287912

TITLE: Ataxin-3 interactions with Rad23 and

valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis

AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran

CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

SOURCE: Molecular and Cellular Biology (2003), 23(18),

6469-6483

CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER:

American Society for Microbiology

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin-3**. We investigated whether **ataxin-3** is a proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin-3** interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin-3** assoc. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin-3** is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:362711 CAPLUS

DOCUMENT NUMBER: 137:92006

TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics

AUTHOR(S): Chen, Songming; Berthelie, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzel, Ronald

CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA

SOURCE: Biochemistry (2002), 41(23), 7391-7399

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington's** disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β -sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	605	pauline.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:14
L2	1158	paulson.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:15
L3	2	l2 and ataxin	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:17
L4	0	ataxin same glutamine same filament	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:17
L5	55	glutamine same filament	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:17
L6	1	glutamine same filament same diameter	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:18
L7	9	(glutamine same repeat) and (filament same diameter)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:44
L8	25	(glutamine same repeat) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:54
L9	4885	(poly(gln) or polyglutamine) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:55
L10	15	("poly(gln)" or polyglutamine) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:56

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'AGRICOLA' ENTERED AT 11:05:58 ON 16 DEC 2004

FILE 'BIOTECHNO' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CONFSCI' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'HEALSAFE' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'IMSDRUGCONF' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (C) 2004 IMSWORLD Publications Ltd.

FILE 'LIFESCI' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'MEDICONF' ENTERED AT 11:05:58 ON 16 DEC 2004
COPYRIGHT (c) 2004 FAIRBASE Datenbank GmbH, Hannover, Germany

FILE 'PASCAL' ENTERED AT 11:05:58 ON 16 DEC 2004
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2004 INIST-CNRS. All rights reserved.

=> (polyglutamine or poly(glu)) and filament and length and diameter
MISSING OPERATOR 'POLY(GLU)'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> (polyglutamine or "poly(glu)") and filament and length and diameter

L1	0 FILE AGRICOLA
L2	0 FILE BIOTECHNO
L3	0 FILE CONFSCI
L4	0 FILE HEALSAFE
L5	0 FILE IMSDRUGCONF
L6	0 FILE LIFESCI
L7	0 FILE MEDICONF
L8	0 FILE PASCAL

TOTAL FOR ALL FILES

L9	0 (POLYGLUTAMINE OR "POLY(GLU)") AND FILAMENT AND LENGTH AND DIAMETER
	TER

=> polyglutamine and filament and length and diameter

L10	0 FILE AGRICOLA
L11	0 FILE BIOTECHNO
L12	0 FILE CONFSCI
L13	0 FILE HEALSAFE
L14	0 FILE IMSDRUGCONF
L15	0 FILE LIFESCI
L16	0 FILE MEDICONF
L17	0 FILE PASCAL

TOTAL FOR ALL FILES

L18	0 POLYGLUTAMINE AND FILAMENT AND LENGTH AND DIAMETER
-----	--

=> polyglutamine and filament and length

L19	0	FILE AGRICOLA
L20	3	FILE BIOTECHNO
L21	0	FILE CONFSCI
L22	0	FILE HEALSAFE
L23	0	FILE IMSDRUGCONF
L24	1	FILE LIFESCI
L25	0	FILE MEDICONF
L26	1	FILE PASCAL

TOTAL FOR ALL FILES

L27 5 POLYGLUTAMINE AND FILAMENT AND LENGTH

=> dup rem

ENTER L# LIST OR (END):l27

DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L27

L28 4 DUP REM L27 (1 DUPLICATE REMOVED)

=> d l28 ibib abs total

L28 ANSWER 1 OF 4 LIFESCI COPYRIGHT 2004 CSA on STN

ACCESSION NUMBER: 2003:45445 LIFESCI

TITLE: Amyloid-like Features of Polyglutamine Aggregates
and Their Assembly Kinetics

AUTHOR: Chen, Songming; Berthelie, V.; Hamilton, J.B.; O'Nuallain,
B.; Wetzel, R.

CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee
Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920,
USA

SOURCE: Biochemistry (Washington) [Biochemistry (Wash.)], (2002)611
) vol. 41, no. 23, pp. 7391-7399.
ISSN: 0006-2960.

DOCUMENT TYPE: Journal

FILE SEGMENT: N3

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The repeat **length**-dependent tendency of the
polyglutamine sequences of certain proteins to form aggregates may
underlie the cytotoxicity of these sequences in expanded CAG repeat
diseases such as Huntington's disease. We report here a number of features
of various **polyglutamine** (polyGln) aggregates and their assembly
pathways that bear a resemblance to generally recognized defining features
of amyloid fibrils. PolyGln aggregation kinetics displays concentration
and **length** dependence and a lag phase that can be abbreviated by
seeding. PolyGln aggregates exhibit classical beta -sheet-rich circular
dichroism spectra consistent with an amyloid-like substructure. The
fundamental structural unit of all the in vitro aggregates described here
is a **filament** about 3 nm in width, resembling the protofibrillar
intermediates in amyloid fibril assembly. We observed these filamentous
structures either as isolated threads, as components of ribbonlike sheets,
or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates
described here bind thioflavin T and shift its fluorescence spectrum.
Although all polyGln aggregates tested bind the dye Congo red, only
aggregates of a relatively long polyGln peptide exhibit Congo red
birefringence, and this birefringence is only observed in a small portion
of these aggregates. Remarkably, a monoclonal antibody with high
selectivity for a generic amyloid fibril conformational epitope is capable
of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of
the characteristic features of amyloid, but the twisted fibril structure
with Congo red birefringence is not the predominant form in the polyGln
repeat **length** range studied here. We also find that polyGln
peptides exhibit an unusual freezing-dependent aggregation that appears to

be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the molecular structure of the product. This ordered structure, or the assembly process leading to it, may be responsible for the cell-specific neuronal degeneration observed in Huntington's and other expanded CAG repeat diseases.

L28 ANSWER 2 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded **polyglutamine** domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO

AB Eight inherited neurodegenerative diseases are caused by genes with expanded CAG repeats coding for **polyglutamine** domains in the disease-producing proteins. The mechanism by which this expanded **polyglutamine** domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic **polyglutamine** protein aggregation is a common feature. In transfected COS7 cells, expanded **polyglutamine** proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-length **polyglutamine** domain proteins also interact with NF. We expressed varying **lengths polyglutamine**-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-length **polyglutamine**-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoprecipitation of pathologic-length **polyglutamine** proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that **polyglutamine** interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L28 ANSWER 3 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1999:30038076 BIOTECHNO
TITLE: **Polyglutamine** domain proteins with expanded repeats bind neurofilament, altering the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Annals of the New York Academy of Sciences, (1999), 893/- (192-202), 49 reference(s)
CODEN: ANYAAO ISSN: 0077-8923
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:30038076 BIOTECHNO
AB Proteins with expanded **polyglutamine** (polyQ) repeats cause eight inherited neurodegenerative diseases. Nuclear and cytoplasmic polyQ protein is a common feature of these diseases, but its role in cell death remains debatable. Since the neuronal intermediate **filament** network is composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic **length** polyQ domain proteins interact with NF. We expressed polyQ-green fluorescent fusion proteins (GFP) in a neuroblast cell line, TR1. Pathologic-**length** polyQ-GFP fusion proteins form large cytoplasmic aggregates surrounded by neurofilament. Immunoprecipitation of pathologic **length** polyQ proteins co-isolated 68 kD NF protein demonstrating molecular interaction. These observations suggest that polyQ interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L28 ANSWER 4 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27464435 BIOTECHNO
TITLE: Oligomerization of expanded-**polyglutamine** domain fluorescent fusion proteins in cultured mammalian cells
AUTHOR: Onodera O.; Burke J.R.; Miller S.E.; Hester S.; Tsuji S.; Roses A.D.; Strittmatter W.J.
CORPORATE SOURCE: W.J. Strittmatter, Department of Medicine (Neurology), Duke University Medical Center, Durham, NC 27710, United States.
E-mail: warren@neuro.duke.edu
SOURCE: Biochemical and Biophysical Research Communications, (1997), 238/2 (599-605), 29 reference(s)
CODEN: BBRCA0 ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1997:27464435 BIOTECHNO
AB Six inherited neurologic diseases, including Huntington's disease, result from the expansion of a CAG domain of the disease genes to produce a domain of more than 40 glutamines in the expressed protein. The mechanism by which expansion of this **polyglutamine** domain causes disease is unknown. Recent studies demonstrated oligomerization of **polyglutamine**-domain proteins in mammalian neurons. To study oligomerization of **polyglutamine** proteins and to identify heterologous protein interactions, varying **length** **polyglutamine**-green fluorescent protein fusion proteins were expressed in cultured COS-7 cells. The 19- and 35-glutamine fusion proteins (non-pathologic **length**) distributed diffusely throughout the cytoplasm. In contrast, 56- and 80-glutamine fusion proteins (pathologic **length**) formed fibrillar arrays resembling those previously observed in neurons in Huntington's disease and in a transgenic mouse model. These aggregates were intranuclear and intracytoplasmic. Intracytoplasmic aggregates were surrounded by collapsed intermediate **filaments**. The intermediate **filament** protein vimentin co-immunoprecipitated with expanded **polyglutamine** fusion proteins. This cellular model will expedite investigations into oligomerization of **polyglutamine** proteins and their interactions with other proteins.

=> wetzel r/au
L29 13 FILE AGRICOLA
L30 38 FILE BIOTECHNO
L31 19 FILE CONFSCI
L32 1 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE

L33 0 FILE IMSDRUGCONF
L34 32 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L35 0 FILE MEDICONF
L36 91 FILE PASCAL

TOTAL FOR ALL FILES

L37 194 WETZEL R/AU

=> yang w/au

L38 61 FILE AGRICOLA
L39 273 FILE BIOTECHNO
L40 107 FILE CONFSCI
L41 5 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE
L42 0 FILE IMSDRUGCONF
L43 175 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L44 0 FILE MEDICONF
L45 356 FILE PASCAL

TOTAL FOR ALL FILES

L46 977 YANG W/AU

=> l37 and l46

L47 0 FILE AGRICOLA
L48 2 FILE BIOTECHNO
L49 0 FILE CONFSCI
L50 0 FILE HEALSAFE
L51 0 FILE IMSDRUGCONF
L52 0 FILE LIFESCI
L53 0 FILE MEDICONF
L54 0 FILE PASCAL

TOTAL FOR ALL FILES

L55 2 L37 AND L46

=> d l55 ibib abs total'

'TOTAL'' IS NOT A VALID FORMAT FOR FILE 'BIOTECHNO'

The following are valid formats:

BIB ----- AN, TI, AU, CS, SO, PUI, DT, CY, LA, SL
IBIB ----- BIB, indented with text labels
ALL ----- AN, TI, AU, CS, SO, PUI, DT, CY, LA, SL, AB, CT, RN, CN, TN, CO, GEN
IALL ----- ALL, indented with text labels
DALL ----- ALL, delimited (end of each field identified)
ABS ----- AN, AB
IND ----- AN, CT, RN, CN, TN, CO, GEN
TRIAL ----- AN, TI, CT
SAM ----- AN, TI, CT
SAMPLE ----- AN, TI, CT
TRI ----- AN, TI, CT

To display a particular field or fields, enter the display field codes. For a list of display field codes, enter 'HELP DFIELDS' at an arrow prompt (=>). Examples of formats include: 'TI'; 'AN,TI,AU'; 'BIB,CT'; 'TI,CT'.

The order of the terms in the formats is not important, but information will be displayed in the same order as the format specification.

The same formats may be used with the DISPLAY AN command to display the record for a specified accession number.

FREE ----- AN, TI, CT
ENTER DISPLAY FORMAT (BIB):bib

AN 2002:35331822 BIOTECHNO
 TI Aggregated polyglutamine peptides delivered to nuclei are toxic to
 mammalian cells
 AU Yang W.; Dunlap J.R.; Andrews R.B.; Wetzel R.
 CS R. Wetzel, Graduate School of Medicine, University of Tennessee Medical
 Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States.
 E-mail: rwetzel@mc.utmck.edu
 SO Human Molecular Genetics, (01 NOV 2002), 11/23 (2905-2917), 51
 reference(s)
 CODEN: HMGEES ISSN: 0964-6906
 DT Journal; Article
 CY United Kingdom
 LA English
 SL English

=> d 155 ibib abs total

L55 ANSWER 1 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 2002:35331822 BIOTECHNO
 TITLE: Aggregated polyglutamine peptides delivered to nuclei
 are toxic to mammalian cells
 AUTHOR: Yang W.; Dunlap J.R.; Andrews R.B.;
 Wetzel R.
 CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, University of
 Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville,
 TN 37920, United States.
 E-mail: rwetzel@mc.utmck.edu
 SOURCE: Human Molecular Genetics, (01 NOV 2002), 11/23
 (2905-2917), 51 reference(s)
 CODEN: HMGEES ISSN: 0964-6906
 DOCUMENT TYPE: Journal; Article
 COUNTRY: United Kingdom
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AN 2002:35331822 BIOTECHNO
 AB A number of observations point to the aggregation of expanded
 polyglutamine [poly(Q)]-containing proteins as playing a central role in
 the etiology of Huntington's disease (HD) and other expanded CAG-repeat
 diseases. Transfected cell and transgenic animal models provide some of
 this support, but irrefutable data on the cytotoxicity of poly(Q)
 aggregates is lacking. This may be due in part to difficulties in
 observing all aggregated states in these models, and in part to the
 inability to conclusively rule out the role of monomeric states of the
 poly(Q) protein. To address these questions, we produced aggregates of
 simple poly(Q) peptides in vitro and introduced them to mammalian cells
 in culture. We find that Cos-7 and PC-12 cells in culture readily take up
 aggregates of chemically synthesized poly(Q) peptides. Simple poly(Q)
 aggregates are localized to the cytoplasm and have little impact on cell
 viability. Aggregates of poly(Q) peptides containing a nuclear
 localization signal, however, are localized to nuclei and lead to
 dramatic cell death. Amyloid fibrils of a non-poly(Q) peptide are
 non-toxic, whether localized to the cytoplasm or nucleus. Nuclear
 localization of an aggregate of a short, Q.sub.2.sub.0, poly(Q) peptide
 is just as toxic as that of a long poly(Q) peptide, supporting the notion
 that the influence of poly(Q) repeat length on disease risk and age of
 onset is at the level of aggregation efficiency. The results support a
 direct role for poly(Q) aggregates in HD-related neurotoxicity.

L55 ANSWER 2 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 2001:32735322 BIOTECHNO
 TITLE: Polyglutamine aggregation behavior in vitro supports a
 recruitment mechanism of cytotoxicity
 AUTHOR: Chen S.; Berthelie V.; Yang W.; Wetzel

CORPORATE SOURCE: R. Wetzels, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzels@mc.utmck.edu

SOURCE: Journal of Molecular Biology, (03 AUG 2001), 311/1 (173-182), 54 reference(s)
CODEN: JMOBAK ISSN: 0022-2836

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2001:32735322 BIOTECHNO

AB In expanded CAG repeat diseases such as Huntington's disease, proteins containing polyglutamine (poly(Gln)) sequences with repeat lengths of about 37 residues or more are associated with development of both disease symptoms and neuronal intranuclear inclusions (NIIs). Disease physiology in animal and cellular models does not always correlate with NII formation, however, and the mechanism by which aggregate formation might lead to cytotoxicity is unknown. To help evaluate various possible mechanisms, we determined the biophysical properties of a series of simple poly(Gln) peptides. The circular dichroism spectra of poly(Gln) peptides with repeat lengths of five, 15, 28 and 44 residues are all nearly identical and are consistent with a high degree of random coil structure, suggesting that the length-dependence of disease is not related to a conformational change in the monomeric states of expanded poly(Gln) sequences. In contrast, there is a dramatic increase in both the kinetics and the thermodynamic favorability of the spontaneous formation of ordered, amyloid-like aggregates for poly(Gln) peptides with repeat lengths of greater than 37 residues. At the same time, poly(Gln) peptides with repeat lengths in the 15-20 residue range, despite their poor abilities to support spontaneous, self-nucleated aggregation, are capable of efficiently adding to an already-formed aggregate. We also find that morphologically small, finely divided aggregates are much more efficient at recruiting poly(Gln) peptides than are large aggregates, suggesting a possible explanation for why disease pathology does not always correlate with the observable NII burden. Together, these data are consistent with a model for disease pathology in which critical cellular proteins possessing poly(Gln) sequences of modest length become inactivated when they are recruited into aggregates of an expanded poly(Gln) protein. .COPYRGHT. 2001 Academic Press.

=> chen s/au

L56 206 FILE AGRICOLA
L57 656 FILE BIOTECHNO
L58 299 FILE CONFSCI
L59 15 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE
L60 0 FILE IMSDRUGCONF
L61 462 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L62 0 FILE MEDICONF
L63 999 FILE PASCAL

TOTAL FOR ALL FILES

L64 2637 CHEN S/AU

=> l64 and repeat and glutamine

L65 0 FILE AGRICOLA
L66 2 FILE BIOTECHNO
L67 0 FILE CONFSCI
L68 0 FILE HEALSAFE
L69 0 FILE IMSDRUGCONF

L70 2 FILE LIFESCI
L71 0 FILE MEDICONF
L72 0 FILE PASCAL

TOTAL FOR ALL FILES

L73 4 L64 AND REPEAT AND GLUTAMINE

=> dup rem

ENTER L# LIST OR (END):173

DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L73

L74 2 DUP REM L73 (2 DUPLICATES REMOVED)

=> d 174 ibib abs total

L74 ANSWER 1 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2003:36183362 BIOTECHNO
TITLE: SCA7 knockin mice model human SCA7 and reveal gradual
accumulation of mutant ataxin-7 in neurons and
abnormalities in short-term plasticity
AUTHOR: Yoo S.-Y.; Pennesi M.E.; Weeber E.J.; Xu B.; Atkinson
R.; **Chen S.**; Armstrong D.L.; Wu S.M.; Sweatt
J.D.; Zoghbi H.Y.
CORPORATE SOURCE: H.Y. Zoghbi, Division of Neuroscience, Baylor College
of Medicine, Houston, TX 77030, United States.
E-mail: hzoghbi@bcm.tmc.edu
SOURCE: Neuron, (06 FEB 2003), 37/3 (383-401), 60 reference(s)
CODEN: NERNET ISSN: 0896-6273
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2003:36183362 BIOTECHNO

AB We targeted 266 CAG **repeats** (a number that causes
infantile-onset disease) into the mouse Sca7 locus to generate an
authentic model of spinocerebellar ataxia type 7 (SCA7). These mice
reproduced features of infantile SCA7 (ataxia, visual impairments, and
premature death) and showed impaired short-term synaptic potentiation;
downregulation of photoreceptor-specific genes, despite apparently normal
CRX activity, led to shortening of photoreceptor outer segments.
Wild-type ataxin-7 was barely detectable, as was mutant ataxin-7 in young
animals; with increasing age, however, ataxin-7 staining became more
pronounced. Neurons that appeared most vulnerable had relatively high
levels of mutant ataxin-7; it is interesting, however, that marked
dysfunction occurred in these neurons weeks prior to the appearance of
nuclear inclusions. These data demonstrate that **glutamine**
expansion stabilizes mutant ataxin-7, provide an explanation for
selective neuronal vulnerability, and show that mutant ataxin-7 impairs
posttetanic potentiation (PTP).

L74 ANSWER 2 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2002:34994493 BIOTECHNO
TITLE: Huntington's disease age-of-onset linked to
polyglutamine aggregation nucleation
AUTHOR: **Chen S.**; Ferrone F.A.; Wetzel R.
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, Univ. of
Tennessee Medical Center, 1924 Alcoa Highway,
Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmc.edu
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (03 SEP 2002), 99/18

(11884-11889), 33 reference(s)
CODEN: PNASA6 ISSN: 0027-8424

DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2002:34994493 BIOTECHNO

AB In Huntington's Disease and related expanded CAG **repeat** diseases, a polyglutamine [poly(Gln)] sequence containing 36 **repeats** in the corresponding disease protein is benign, whereas a sequence with only 2-3 additional **glutamines** is associated with disease risk. Above this threshold range, longer **repeat** lengths are associated with earlier ages-of-onset. To investigate the biophysical basis of these effects, we studied the in vitro aggregation kinetics of a series of poly(Gln) peptides. We find that poly(Gln) peptides in solution at 37°C undergo a random coil to β -sheet transition with kinetics superimposable on their aggregation kinetics, suggesting the absence of soluble, β -sheet-rich intermediates in the aggregation process. Details of the time course of aggregate growth confirm that poly(Gln) aggregation occurs by nucleated growth polymerization. Surprisingly, however, and in contrast to conventional models of nucleated growth polymerization of proteins, we find that the aggregation nucleus is a monomer. That is, nucleation of poly(Gln) aggregation corresponds to an unfavorable protein folding reaction. Using parameters derived from the kinetic analysis, we estimate the difference in the free energy of nucleus formation between benign and pathological length poly(Gln)s to be less than 1 kcal/mol. We also use the kinetic parameters to calculate predicted aggregation curves for very low concentrations of poly(Gln) that might obtain in the cell. The **repeat** -length-dependent differences in predicted aggregation lag times are in the same range as the length-dependent age-of-onset differences in Huntington's disease, suggesting that the biophysics of poly(Gln) aggregation nucleation may play a major role in determining disease onset.

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1641cxc

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 01 New pricing for the Save Answers for SciFinder Wizard within
STN Express with Discover!
NEWS 4 OCT 28 KOREAPAT now available on STN
NEWS 5 NOV 18 Current-awareness alerts, saved answer sets, and current
search transcripts to be affected by CERAB, COMPUAB, ELCOM,
and SOLIDSTATE reloads
NEWS 6 NOV 30 PHAR reloaded with additional data
NEWS 7 DEC 01 LISA now available on STN
NEWS 8 DEC 09 12 databases to be removed from STN on December 31, 2004
NEWS 9 DEC 15 MEDLINE update schedule for December 2004

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 11:36:11 ON 16 DEC 2004

=> file .chemistry
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 11:36:24 ON 16 DEC 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOTECHNO' ENTERED AT 11:36:24 ON 16 DEC 2004

COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'COMPENDEX' ENTERED AT 11:36:24 ON 16 DEC 2004
Compendex Compilation and Indexing (C) 2004
Elsevier Engineering Information Inc (EEI). All rights reserved!
Compendex (R) is a registered Trademark of Elsevier Engineering Information Inc.

FILE 'ANABSTR' ENTERED AT 11:36:24 ON 16 DEC 2004
COPYRIGHT (c) 2004 THE ROYAL SOCIETY OF CHEMISTRY (RSC)

FILE 'CERAB' ENTERED AT 11:36:24 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'METADEX' ENTERED AT 11:36:24 ON 16 DEC 2004
COPYRIGHT (c) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'USPATFULL' ENTERED AT 11:36:24 ON 16 DEC 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> chen s/au

L1	911	FILE CAPLUS
L2	656	FILE BIOTECHNO
L3	530	FILE COMPENDEX
L4	155	FILE ANABSTR
L5	0	FILE CERAB
L6	421	FILE METADEX
L7	0	FILE USPATFULL

TOTAL FOR ALL FILES

L8	2673	CHEN S/AU
----	------	-----------

=> wetzel r/au

L9	69	FILE CAPLUS
L10	38	FILE BIOTECHNO
L11	17	FILE COMPENDEX
L12	5	FILE ANABSTR
L13	0	FILE CERAB
L14	3	FILE METADEX
L15	0	FILE USPATFULL

TOTAL FOR ALL FILES

L16	132	WETZEL R/AU
-----	-----	-------------

=> l8 and l16

L17	0	FILE CAPLUS
L18	4	FILE BIOTECHNO
L19	0	FILE COMPENDEX
L20	1	FILE ANABSTR
L21	0	FILE CERAB
L22	0	FILE METADEX
L23	0	FILE USPATFULL

TOTAL FOR ALL FILES

L24	5	L8 AND L16
-----	---	------------

=> d l24 ibib abs total

L24 ANSWER 1 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2002:34994493 BIOTECHNO

TITLE: Huntington's disease age-of-onset linked to
polyglutamine aggregation nucleation

AUTHOR: Chen S.; Ferrone F.A.; Wetzel R.

CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, Univ. of
Tennessee Medical Center, 1924 Alcoa Highway,
Knoxville, TN 37920, United States.

E-mail: rwetzel@mc.utmck.edu

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (03 SEP 2002), 99/18
(11884-11889), 33 reference(s)
CODEN: PNASA6 ISSN: 0027-8424

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2002:34994493 BIOTECHNO

AB In Huntington's Disease and related expanded CAG repeat diseases, a polyglutamine [poly(Gln)] sequence containing 36 repeats in the corresponding disease protein is benign, whereas a sequence with only 2-3 additional glutamines is associated with disease risk. Above this threshold range, longer repeat lengths are associated with earlier ages-of-onset. To investigate the biophysical basis of these effects, we studied the in vitro aggregation kinetics of a series of poly(Gln) peptides. We find that poly(Gln) peptides in solution at 37°C undergo a random coil to β -sheet transition with kinetics superimposable on their aggregation kinetics, suggesting the absence of soluble, β -sheet-rich intermediates in the aggregation process. Details of the time course of aggregate growth confirm that poly(Gln) aggregation occurs by nucleated growth polymerization. Surprisingly, however, and in contrast to conventional models of nucleated growth polymerization of proteins, we find that the aggregation nucleus is a monomer. That is, nucleation of poly(Gln) aggregation corresponds to an unfavorable protein folding reaction. Using parameters derived from the kinetic analysis, we estimate the difference in the free energy of nucleus formation between benign and pathological length poly(Gln)s to be less than 1 kcal/mol. We also use the kinetic parameters to calculate predicted aggregation curves for very low concentrations of poly(Gln) that might obtain in the cell. The repeat-length-dependent differences in predicted aggregation lag times are in the same range as the length-dependent age-of-onset differences in Huntington's disease, suggesting that the biophysics of poly(Gln) aggregation nucleation may play a major role in determining disease onset.

L24 ANSWER 2 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2001:32756978 BIOTECHNO

TITLE: A microtiter plate assay for polyglutamine aggregate extension

AUTHOR: Bertheliev V.; Hamilton J.B.; **Chen S.**;
Wetzel R.

CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, R221, Univ. of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.

SOURCE: Analytical Biochemistry, (15 AUG 2001), 295/2
(227-236), 43 reference(s)
CODEN: ANBCA2 ISSN: 0003-2697

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2001:32756978 BIOTECHNO

AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded CAG repeat disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln

peptide. Europium-streptavidin complexation of the immobilized biotin, followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the assembly mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln length dependence. The assay also will be a valuable tool for screening and characterizing antiaggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism. .COPYRG. 2001 Academic Press.

L24 ANSWER 3 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32735322 BIOTECHNO
TITLE: Polyglutamine aggregation behavior in vitro supports a recruitment mechanism of cytotoxicity
AUTHOR: Chen S.; Berthelie V.; Yang W.; Wetzl R.
CORPORATE SOURCE: R. Wetzl, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzl@mc.utmck.edu
SOURCE: Journal of Molecular Biology, (03 AUG 2001), 311/1 (173-182), 54 reference(s)
CODEN: JMOBAK ISSN: 0022-2836
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2001:32735322 BIOTECHNO
AB In expanded CAG repeat diseases such as Huntington's disease, proteins containing polyglutamine (poly(Gln)) sequences with repeat lengths of about 37 residues or more are associated with development of both disease symptoms and neuronal intranuclear inclusions (NIIs). Disease physiology in animal and cellular models does not always correlate with NII formation, however, and the mechanism by which aggregate formation might lead to cytotoxicity is unknown. To help evaluate various possible mechanisms, we determined the biophysical properties of a series of simple poly(Gln) peptides. The circular dichroism spectra of poly(Gln) peptides with repeat lengths of five, 15, 28 and 44 residues are all nearly identical and are consistent with a high degree of random coil structure, suggesting that the length-dependence of disease is not related to a conformational change in the monomeric states of expanded poly(Gln) sequences. In contrast, there is a dramatic increase in both the kinetics and the thermodynamic favorability of the spontaneous formation of ordered, amyloid-like aggregates for poly(Gln) peptides with repeat lengths of greater than 37 residues. At the same time, poly(Gln) peptides with repeat lengths in the 15-20 residue range, despite their poor abilities to support spontaneous, self-nucleated aggregation, are capable of efficiently adding to an already-formed aggregate. We also find that morphologically small, finely divided aggregates are much more efficient at recruiting poly(Gln) peptides than are large aggregates, suggesting a possible explanation for why disease pathology does not always correlate with the observable NII burden. Together, these data are consistent with a model for disease pathology in which critical cellular proteins possessing poly(Gln) sequences of modest length become inactivated when they are recruited into aggregates of an expanded poly(Gln) protein. .COPYRG. 2001 Academic Press.

L24 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32240515 BIOTECHNO
TITLE: Solubilization and disaggregation of polyglutamine peptides
AUTHOR: Chen S.; Wetzl R.

CORPORATE SOURCE: Dr. R. Wetzel, Graduate School of Medicine, R221 Univ.
of Tennessee Med. Center, 1924 Alcoa Highway,
Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Protein Science, (2001), 10/4 (887-891), 16
reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2001:32240515 BIOTECHNO

AB A method is described for dissolving and disaggregating chemically synthesized polyglutamine peptides. Polyglutamine peptides longer than about Q.sub.2.sub.0 have been reported to be insoluble in water, but dissolution in - and evaporation from - a mixture of trifluoroacetic acid and hexafluoroisopropanol converts polyglutamine peptides up to at least Q.sub.4.sub.4 to a form readily soluble in aqueous buffers. This procedure also has a dramatic effect on peptides which appear to be completely soluble in water, by removing traces of aggregate that seed aggregation. The protocol makes possible solution studies - including in vitro aggregation experiments - on polyglutamine peptides with repeat lengths associated with increased risk of Huntington's Disease and other expanded CAG repeat diseases. It may also be useful in conducting reproducible, quantitative aggregation studies on other polypeptides.

L24 ANSWER 5 OF 5 ANABSTR COPYRIGHT 2004 RSC on STN

AB In connection the development of an assay for "extension-competent" or "seeding-competent" polyglutamine aggregates in tissue or serum, up to 5 ng portions of synthetic polyglutamine aggregates (SPA) were immobilized in microtitre-plate wells and incubated first with a standard amount of biotinylated SPA and then with Eu-streptavidin complex. The amount of Eu bound was measured by time-resolved fluorimetry and converted into the amount of biotinylated SPA on the basis of the association of seven Eu³⁺ with each molecule of streptavidin. The amount of biotinylated SPA bound varied linearly with the amount of SPA immobilized on the plate; the detection limit was 80 pg.

here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington's** and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 3 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 1999:29124713 BIOTECHNO
 TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network
 AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
 CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
 SOURCE: E-mail: james.burke@duke.edu
 Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
 CODEN: EXNEAC ISSN: 0014-4886
 DOCUMENT TYPE: Journal; Article
 COUNTRY: United States
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO
 AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length** polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length** polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoprecipitation of pathologic-**length** polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

=> file .meeting

'EVENTLINE' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE):ignore

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
49.60	56.85

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

-1.40

-1.40

FILE 'AGRICOLA' ENTERED AT 15:24:54 ON 16 DEC 2004

FILE 'BIOTECHNO' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CONFSCI' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'HEALSAFE' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'IMSDRUGCONF' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 IMSWORLD Publications Ltd.

FILE 'LIFESCI' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'MEDICONF' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (c) 2004 FAIRBASE Datenbank GmbH, Hannover, Germany

FILE 'PASCAL' ENTERED AT 15:24:54 ON 16 DEC 2004

Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.

COPYRIGHT (C) 2004 INIST-CNRS. All rights reserved.

=> amyloid and (filament or aggregate or assembly) and length and diameter

L35	1 FILE AGRICOLA
L36	4 FILE BIOTECHNO
L37	0 FILE CONFSCI
L38	0 FILE HEALSAFE
L39	0 FILE IMSDRUGCONF
L40	3 FILE LIFESCI
L41	0 FILE MEDICONF
L42	1 FILE PASCAL

TOTAL FOR ALL FILES

L43	9 AMYLOID AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH AND DIAMETER
-----	---

=> dup rem

ENTER L# LIST OR (END):l43

DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L43

L44	5 DUP REM L43 (4 DUPLICATES REMOVED)
-----	--------------------------------------

=> d l44 ibib abs total

L44 ANSWER 1 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2003:37345999 BIOTECHNO

TITLE: Architecture of Ure2p Prion **Filaments**: The
N-terminal domains form a central core fiber

AUTHOR: Baxa U.; Taylor K.L.; Wall J.S.; Simon M.N.; Cheng N.;
Wickner R.B.; Steven A.C.

CORPORATE SOURCE: A.C. Steven, Bldg. 50, MSC 8025, 50 South Dr.,
Bethesda, MD 20892-8025, United States.

SOURCE: E-mail: Alasdair_Steven@nih.gov
Journal of Biological Chemistry, (31 OCT 2003), 278/44
(43717-43727), 46 reference(s)

CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 2003:37345999 BIOTECHNO

AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p determines its in vivo prion properties and in vitro **amyloid**-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diameter Ure2p filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diameters** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning transmission electron microscopy (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

L44 ANSWER 2 OF 5 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved.
(2004) on STN DUPLICATE 1

ACCESSION NUMBER: 2002:50889 AGRICOLA

DOCUMENT NUMBER: IND23281705

TITLE: Mechanism of inactivation on prion conversion of the *Saccharomyces cerevisiae* Ure2 protein.

AUTHOR(S): Baxa, U.; Speransky, V.; Steven, A.C.; Wickner, R.B.

AVAILABILITY: DNAL (500 N21P)

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Apr 16, 2002. Vol. 99, No. 8. p. 5253-5260

Publisher: Washington, D.C. : National Academy of Sciences,

CODEN: PNASAG; ISSN: 0027-8424

NOTE: Includes references

PUB. COUNTRY: District of Columbia; United States

DOCUMENT TYPE: Article; Conference

FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension

LANGUAGE: English

AB The [URE3] infectious protein (prion) of *Saccharomyces cerevisiae* is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diameters** increased with the mass of the appended enzyme. The

helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all beta-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

L44 ANSWER 3 OF 5 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 2
 ACCESSION NUMBER: 1999:39603 LIFESCI
 TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
 AUTHOR: Taylor, K.L.; Cheng, Naiqian; Williams, R.W.; Steven, A.C.; Wickner, R.B.*
 CORPORATE SOURCE: Lab. Biochem. and Genet., Natl. Inst. Health, Bethesda, MD 20892-0830, USA; E-mail: wickner@helix.nih.gov
 SOURCE: Science (Washington) [Science (Wash.)], (19990226) vol. 283, no. 5406, pp. 1339-1343. ISSN: 0036-8075.
 DOCUMENT TYPE: Journal
 FILE SEGMENT: K; V
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB The [URE3] non-Mendelian genetic element of *Saccharomyces cerevisiae* is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p super(1-65) were shown to polymerize to form **filaments** 40 to 45 angstroms in **diameter** with more than 60 percent beta sheet. Ure2p specifically induced full-**length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in extracts of [URE3] strains, these 180- to 220-angstrom-**diameter filaments** were protease resistant. The Ure2p super(1-65)-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular **filaments**. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].

L44 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 1991:21180842 BIOTECHNO
 TITLE: Morphology and antibody recognition of synthetic β - **amyloid** peptides
 AUTHOR: Fraser P.E.; Duffy L.K.; O'Malley M.B.; Nguyen J.; Inouye H.; Kirschner D.A.
 CORPORATE SOURCE: Neurology Research, Children's Hospital, Enders 2, 320 Longwood Ave., Boston, MA 02115, United States.
 SOURCE: Journal of Neuroscience Research, (1991), 28/4 (474-485)
 CODEN: JNREDK ISSN: 0360-4012
 DOCUMENT TYPE: Journal; Article
 COUNTRY: United States
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AN 1991:21180842 BIOTECHNO
 AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β -**amyloid** protein (β -AP), we investigated the ability of peptides sharing sequences with β -AP to form fibrils in vitro and to recognize anti- β - **amyloid** antisera. The peptides, which

were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β -AP. Electron microscopy of negative-stained or thin-sectioned preparations revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diameters** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diameters** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1,100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diameter**. When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross- β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β -(1-28) was highly reactive in an inhibition-ELISA assay to β -(6-25) and β -(1-38), but not to β -(22-35), and immunostained β -(1-40) on Western blots. These studies show that the β -(6-25), β -(1-38) and β -(1-40) peptides can assemble into cross- β fibrils that retain epitopes characteristic of AD **amyloid**.

L44 ANSWER 5 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1985:15068440 BIOTECHNO
TITLE: Identification of prion **amyloid**
filaments in scrapie-infected brain
AUTHOR: DeArmond S.J.; McKinley M.P.; Barry R.A.; et al.
CORPORATE SOURCE: Department of Pathology, University of California, San
Francisco, CA 94143, United States.
SOURCE: Cell, (1985), 41/1 (221-235)
CODEN: CELLB5
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English

AN 1985:15068440 BIOTECHNO

AB Extracellular collections of abnormal **filaments** composed of prion proteins have been identified in the brains of scrapie-infected hamsters using immuno-electron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, and determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

=> file .jacob
COST IN U.S. DOLLARS
FULL ESTIMATED COST

SINCE FILE	TOTAL
ENTRY	SESSION
19.73	76.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.40

FILE 'CAPLUS' ENTERED AT 15:31:45 ON 16 DEC 2004
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:31:45 ON 16 DEC 2004
 Copyright (c) 2004 The Thomson Corporation.

FILE 'MEDLINE' ENTERED AT 15:31:45 ON 16 DEC 2004

FILE 'EMBASE' ENTERED AT 15:31:45 ON 16 DEC 2004
 COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'USPATFULL' ENTERED AT 15:31:45 ON 16 DEC 2004
 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregate or assembly) and length

L45	2 FILE CAPLUS
L46	4 FILE BIOSIS
L47	1 FILE MEDLINE
L48	2 FILE EMBASE
L49	50 FILE USPATFULL

TOTAL FOR ALL FILES

L50	59 (CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH
-----	--

=> dup rem

ENTER L# LIST OR (END):145-148

PROCESSING COMPLETED FOR L45

PROCESSING COMPLETED FOR L46

PROCESSING COMPLETED FOR L47

PROCESSING COMPLETED FOR L48

L51 5 DUP REM L45-L48 (4 DUPLICATES REMOVED)

=> d l51 ibib abs total

L51 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:716876 CAPLUS

DOCUMENT NUMBER: 139:287912

TITLE: **Ataxin-3** interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis

AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran

CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

SOURCE: Molecular and Cellular Biology (2003), 23(18), 6469-6483

CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin-3**. We investigated whether **ataxin-3** is a

proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin-3** interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin-3** assoc. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin-3** is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:278678 BIOSIS
DOCUMENT NUMBER: PREV200200278678
TITLE: Remedy for **CAG repeat** expansion diseases.
AUTHOR(S): Tsuji, Shoji [Inventor, Reprint author]
CORPORATE SOURCE: Niigata, Japan
ASSIGNEE: Niigata University, Japan
PATENT INFORMATION: US 6355690 March 12, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 12, 2002) Vol. 1256, No. 2.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB To elucidate the molecular mechanisms of "gain of toxic function" of expanded polyglutamine stretches in **CAG repeat** expansion diseases, the inventors established an expression system of full-**length** and truncated cDNAs for dentatorubral-pallidoluysian atrophy (**DRPLA**) and found that truncated **DRPLA** proteins containing the expanded polyglutamine stretch, but not the full-**length** protein, form peri- and intra-nuclear aggregates consisting of **filaments** and concomitant apoptosis. The apoptotic cell death was partially suppressed by transglutaminase inhibitors, cystamine and monodansyl cadaverine, raising the possibility of involvement of transglutaminase reaction. The results may provide a potential basis for the development of therapeutic measures for **CAG repeat** expansion diseases.

L51 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelie, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzell, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the

cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington's** disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β -sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington's** and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
 ACCESSION NUMBER: 2001:433998 BIOSIS
 DOCUMENT NUMBER: PREV200100433998
 TITLE: A microtiter plate assay for polyglutamine aggregate extension.
 AUTHOR(S): Berthelie, Valerie; Hamilton, J. Bradley; Chen, Songming; Wetzel, Ronald [Reprint author]
 CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, R221, Knoxville, TN, 37920, USA
 SOURCE: Analytical Biochemistry, (August 15, 2001) Vol. 295, No. 2, pp. 227-236. print.
 CODEN: ANBCA2. ISSN: 0003-2697.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 12 Sep 2001
 Last Updated on STN: 22 Feb 2002

AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded **CAG repeat** disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln peptide. Europium-streptavidin complexation of the immobilized biotin,

followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the **assembly** mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln **length** dependence. The assay also will be a valuable tool for screening and characterizing anti-aggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism.

L51 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
DUPLICATE 2

ACCESSION NUMBER: 1999:180905 BIOSIS
DOCUMENT NUMBER: PREV199900180905
TITLE: Expanded polyglutamine domain proteins bind neurofilament
and alter the neurofilament network.
AUTHOR(S): Nagai, Yoshitaka; Onodera, Osamu; Chun, Jerold;
Strittmatter, Warren J.; Burke, James R. [Reprint author]
CORPORATE SOURCE: Department of Medicine (Neurology), Duke University Medical
Center, Durham, NC, 27710, USA
SOURCE: Experimental Neurology, (Feb., 1999) Vol. 155, No. 2, pp.
195-203. print.
CODEN: EXNEAC. ISSN: 0014-4886.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

AB Eight inherited neurodegenerative diseases are caused by genes with
expanded **CAG repeats** coding for polyglutamine domains
in the disease-producing proteins. The mechanism by which this expanded
polyglutamine domain causes neurodegenerative disease is unknown, but
nuclear and cytoplasmic polyglutamine protein aggregation is a common
feature. In transfected COS7 cells, expanded polyglutamine proteins
aggregate and disrupt the vimentin intermediate **filament**
network. Since neurons have an intermediate **filament** network
composed of neurofilament (NF) and NF abnormalities occur in
neurodegenerative diseases, we examined whether pathologic-**length**
polyglutamine domain proteins also interact with NF. We expressed varying
lengths polyglutamine-green fluorescent protein fusion proteins in
a neuroblast cell line, TR1. Pathologic-**length**
polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates
surrounded by neurofilament. Immunolocalization of pathologic-**length**
polyglutamine proteins coisolated 68-kDa NF protein demonstrating
molecular interaction. These observations suggest that polyglutamine
interaction with NF is important in the pathogenesis of the polyglutamine
repeat diseases.

=> amyloid and (filament or aggregate or assembly) and length and diameter

L52 11 FILE CAPLUS
L53 8 FILE BIOSIS
L54 9 FILE MEDLINE
L55 10 FILE EMBASE
L56 793 FILE USPATFULL

TOTAL FOR ALL FILES

L57 831 AMYLOID AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH AND
DIAMETER

=> dup rem

ENTER L# LIST OR (END):152-155

PROCESSING COMPLETED FOR L52

PROCESSING COMPLETED FOR L53

PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L55
L58 16 DUP REM L52-L55 (22 DUPLICATES REMOVED)

=> d l58 ibib abs total

L58 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:495393 CAPLUS

DOCUMENT NUMBER: 141:201912

TITLE: The formation of straight and twisted

filaments from short tau peptides

AUTHOR(S): Goux, Warren J.; Kopplin, Lauren; Nguyen, Anh D.;
Leak, Kathryn; Rutkofsky, Marni; Shanmuganandam,
Vasanthi D.; Sharma, Deepak; Inouye, Hideyo;
Kirschner, Daniel A.

CORPORATE SOURCE: Department of Chemistry, the University of Texas at
Dallas, Richardson, TX, 75083-0688, USA

SOURCE: Journal of Biological Chemistry (2004), 279(26),
26868-26875

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We studied fibril formation in a family of peptides based on PHF6 (VQIVYK), a short peptide segment found in the microtubule binding region of tau protein. N-Acetylated peptides AcVYK-amide (AcVYK), AcIVYK-amide (AcPHF4), AcQIVYK-amide (AcPHF5), and AcV-QIVYK-amide (AcPHF6) rapidly formed straight **filaments** in the presence of 0.15 M NaCl, each composed of two laterally aligned protofilaments .apprx.5 nm in width. X-ray fiber diffraction showed the omnipresent sharp 4.7-Å reflection indicating that the scattering objects are likely elongated along the hydrogen-bonding direction in a cross-β conformation, and Fourier transform IR suggested the peptide chains were in a parallel (AcVYK, AcPHF6) or antiparallel (AcPHF4, AcPHF5) β-sheet configuration. The dipeptide N-acetyl-YK-amide (AcYK) formed globular structures .apprx.200 nm to 1 μm in **diam**. The polymerization rate, as measured by thioflavin S binding, increased with the **length** of the peptide going from AcYK → AcPHF6, and peptides that aggregated most rapidly displayed CD spectra consistent with β-sheet structure. There was a 3-fold decrease in rate when Val was substituted for Ile or Gln, nearly a 10-fold decrease when Ala was substituted for Tyr, and an increase in polymerization rate when Glu was substituted for Lys. Twisted **filaments**, composed of four laterally aligned protofilaments (9-19 nm width, .apprx.90 nm half-periodicity), were formed by mixing AcPHF6 with AcVYK. Taken together these results suggest that the core of PHF6 is localized at VYK, and the interaction between small amphiphilic segments of tau may initiate nucleation and lead to **filaments** displaying paired helical **filament** morphol.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN

ACCESSION NUMBER: 2004:160995 BIOSIS

DOCUMENT NUMBER: PREV200400164922

TITLE: Formation of **amyloid** from superoxide dismutase.

AUTHOR(S): Oztug, Zeynep [Reprint Author]; Padua, Shelby [Reprint
Author]; Downes, Sean [Reprint Author]; Cohlberg, Jeffrey
A. [Reprint Author]; Rodriguez, Jorge; Doucette, Peter;
Valentine, Joan S.

CORPORATE SOURCE: Dept of Chemistry and Biochemistry, California State
University, Long Beach, Long Beach, CA, USA

SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

504a. print.

Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.

ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 24 Mar 2004

Last Updated on STN: 24 Mar 2004

AB Mutations in copper-zinc superoxide dismutase (SOD) are the cause of 20 percent of the cases of familial amyotrophic lateral sclerosis (FALS). Insoluble deposits containing SOD are found in motor neurons of FALS patients, some of which are reactive with the **amyloid**-specific dye thioflavin S. It has been proposed that the mutations cause the disease by increasing the tendency of SOD to aggregate. Furthermore, certain SOD crystal structures show linear arrays of SOD dimers similar to **amyloid filaments**. Therefore, conditions were sought under which SOD forms **amyloid**. Protein solutions were agitated at 37C in the presence of thioflavin T, and **amyloid** formation was detected by monitoring fluorescence with a microplate reader. Wild-type SOD formed **amyloid** at pH 3 and 0.5-2 M guanidine hydrochloride, with an optimum of about 1 M guanidine. The kinetics showed a lag phase of variable **length**, typically about 24 hr, followed by a rise in fluorescence over a period of a few hours. Incubation of the product with Congo Red produced a shift in the absorbance peak from 510 nm to 542 nm. Transmission electron microscopy revealed straight **filaments** with **diameters** of about 10 nm, often appearing as bundles up to 50 nm in **diameter**. Apo-SOD did not form **amyloid** under these conditions. Various FALS-related mutant SODs also formed **amyloid filaments** at acidic pH and low concentrations of guanidine. For some of the mutants less acidic conditions were required to promote **amyloid** formation. Under some conditions, mutant SODs formed **amyloid** only when seeded by preexisting **amyloid**, while seeding appeared to have no effect with other samples. 30% acetonitrile can substitute for guanidine hydrochloride in promoting **amyloid** formation. The results may be relevant to the aggregation of SOD which occurs in motor neurons in FALS.

L58 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:660806 CAPLUS

TITLE: Nanostructure of β -sheet fibrils constructed by unfolded β -hairpin peptide self- **assembly**

AUTHOR(S): Lamm, Matthew S.; Rajagopal, Karthikan; Schneider, Joel P.; Pochan, Darrin J.

CORPORATE SOURCE: Department of Materials Science and Engineering, University of Delaware, Newark, DE, 19716, USA

SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), POLY-345. American Chemical Society: Washington, D. C.

CODEN: 69FTZ8

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB A 20-residue peptide consisting of alternating valine and lysine residues flanking a tripeptide turn sequence has been shown to self-assemble via differing pathways into dramatically different materials, depending on the primary structure of the turn sequence. Under appropriate solution conditions, peptides with type II' turn sequences intramolecularly fold leading to β -sheet rich, reversible hydrogelation. Alternatively, almost identical peptides, differing only in turn sequence that strongly disfavors intramol. folding, adopt an extended β -sheet conformation and irreversibly assemble into β - **amyloid**-like, prion-like

fibrillar structures. The resulting fibrillar structures are analyzed using transmission electron microscopy, atomic force microscopy and x-ray diffraction; an untwisted, un-branched morphol. is observed characterized by lateral **assembly** of .apprx.2.5nm **diam.** **filaments** and up to microns in **length**. Lateral association of **filaments** produced fibril widths of 100nm or more. Each fibril has an exact height of .apprx.6.7nm suggesting that each peptide is in an extended conformation with the peptide backbone orthogonal to both the fibril axis and the direction of lamination.

L58 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:850847 CAPLUS

DOCUMENT NUMBER: 140:2085

TITLE: Architecture of Ure2p Prion **Filaments**: the N-terminal domains form a central core fiber

AUTHOR(S): Baxa, Ulrich; Taylor, Kimberly L.; Wall, Joseph S.; Simon, Martha N.; Cheng, Naiqian; Wickner, Reed B.; Steven, Alasdair C.

CORPORATE SOURCE: Lab. Struct. Biol., Natl. Inst. Arthritis, Musculoskeletal, and Skin Dis., Natl. Inst. Health, Bethesda, MD, 20892, USA

SOURCE: Journal of Biological Chemistry (2003), 278(44), 43717-43727

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p det. its in vivo prion properties and in vitro **amyloid-forming** ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diam.** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diam.** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning TEM (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:72748 CAPLUS

DOCUMENT NUMBER: 136:146104

TITLE: Human stress genes identified using DNA microarrays

INVENTOR(S): Chenchik, Alex; Lukashev, Matvey E.

PATENT ASSIGNEE(S): Clontech, USA

SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 441,920.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002009730	A1	20020124	US 2001-782909	20010213
PRIORITY APPLN. INFO.:			US 1998-222256	B2 19981228
			US 1999-440305	B2 19991117
			US 1999-441920	A2 19991117

AB Human stress arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe composition of unique polynucleotides corresponding to a human stress gene. The average **length** of the polynucleotide probes is between 50 to 1000 nucleotides. The d. of the spots on the array did not exceed 400/cm2 and the spots had a **diam** . ranging between 10 to 5000 μ m. Furthermore, the number of polynucleotide probe spots on the array ranged between 50 to 2000 nucleotides. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of human stress genes. 236 Different human stress genes were identified using this approach.

L58 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:316601 CAPLUS

DOCUMENT NUMBER: 137:45099

TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein

AUTHOR(S): Baxa, Ulrich; Speransky, Vladislav; Steven, Alasdair C.; Wickner, Reed B.

CORPORATE SOURCE: Laboratories of Structural Biology, National Institute of Arthritis, Musculoskeletal Diseases, and Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(8), 5253-5260
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich N-terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diam**s . increased with the mass of the appended enzyme. The helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all β -sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:703452 CAPLUS
DOCUMENT NUMBER: 138:2785
TITLE: Examining the structure of the mature amyloid fibril
AUTHOR(S): Makin, O. S.; Serpell, L. C.
CORPORATE SOURCE: Structural Medicine Unit, Cambridge Institute for Medical Research, Cambridge, CB2 2XY, UK
SOURCE: Biochemical Society Transactions (2002), 30(4), 521-525
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The pathogenesis of the group of diseases known collectively as the amyloidoses is characterized by the deposition of insol. amyloid fibrils. These are straight, unbranching structures about 70-120 Å (1 Å = 0.1 nm) in diam. and of indeterminate length formed by the self-assembly of a diverse group of normally soluble proteins. Knowledge of the structure of these fibrils is necessary for the understanding of their abnormal assembly and deposition, possibly leading to the rational design of therapeutic agents for their prevention or disaggregation. Structural elucidation is impeded by fibril insol. and inability to crystallize, thus preventing the use of x-ray crystallog. and solution NMR. CD, Fourier-transform IR spectroscopy and light scattering have been used in the study of the mechanism of fibril formation. This review concs. on the structural information about the final, mature fibril and in particular the complementary techniques of cryo-electron microscopy, solid-state NMR and x-ray fiber diffraction.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001241576 EMBASE
TITLE: Yeast prions act as genes composed of self-propagating protein amyloids.
AUTHOR: Wickner R.B.; Taylor K.L.; Edskes H.K.; Maddelein M.-L.; Moriyama H.; Tibor Roberts B.
CORPORATE SOURCE: R.B. Wickner, Laboratory of Biochemistry, Natl. Inst. Diab. Digest./Kid. Dis., National Institutes of Health, Bethesda, MD 20892, United States
SOURCE: Advances in Protein Chemistry, (2001) 57/- (313-334).
Refs: 71
ISSN: 0065-3233 CODEN: APCHA2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We proposed genetic properties by which prions can be recognized among infectious elements. This indicated that [URE3] and [PSI], two nonchromosomal genetic elements of yeast, were prions (infectious altered forms) of Ure2p and Sup35p, respectively. Overexpression of Ure2p leads to the de novo appearance of the [URE3] prion, and the N-terminal 65-80 residues (the prion domain) are specifically responsible for this prion-inducing activity. The prion domain is sufficient to propagate [URE3] and is necessary for a Ure2p molecule to be affected by [URE3]. The remaining C-terminal residues 81-354 are responsible for nitrogen catabolite repression, the normal function of Ure2p. Ure2p is protease-resistant specifically in extracts of [URE3] strains and is

aggregated in vivo specifically in such strains. The chemically synthesized Ure2p prion domain (Ure2p(1-65)) spontaneously forms classic **amyloid filaments** (50 A diameter) in vitro, and specifically induces the native full length Ure2p to form a 1:1 **amyloid** cofilament (200 A). These **amyloid** cofilaments can prime amyloid **filament** formation by an excess of native Ure2p. The features of the in vitro **amyloid** propagation reaction appear to reproduce the in vivo properties of [URE3] prion propagation. This system may be useful for detecting new prions, finding **amyloid**-inducing and **amyloid**-curing agents, and determining the cellular components that affect the initiation and propagation of infectious **amyloids**. The [Het-s] prion was found in the filamentous fungus *Podospora anserina* by similar genetic tests to those we used for [URE3] and [PSI]. [Het-s] is necessary for a normal function of *Podospora* cells, heterokaryon incompatibility. This suggests that other normal cellular functions may involve a prion-like mechanism.

L58 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:80946 BIOSIS
DOCUMENT NUMBER: PREV200100080946
TITLE: A de novo designed helix-turn-helix peptide forms nontoxic **amyloid** fibrils.
AUTHOR(S): Fezoui, Y. [Reprint author]; Hartley, D. M.; Walsh, D. M.; Selkoe, D. J.; Osterhout, J. J.; Teplow, D. B.
CORPORATE SOURCE: Brigham and Women's Hospital, Boston, MA, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-299.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract).
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

AB During fibrillogenesis studies of the **amyloid** beta-protein (Abeta), we sought a non-amyloidogenic "negative control" peptide. Prior work suggested that alphata1, a de novo designed, monomeric, 38-residue alpha-helix-turn-alpha-helix peptide would be ideal. alphata1 was developed as a model for the study of protein folding intermediates and has a protein-like sequence and a stable tertiary structure. At pH 3.6 and pH 10.5, alphata1 showed no aggregation after 8 weeks of incubation at 37degreeC. Surprisingly, at neutral pH, alphata1 formed fibrils after 2 days of incubation at 37degreeC. Negative staining and electron microscopy revealed non-branching fibril **assemblies** 6-10 nm in width, which varied in length from 200 to 1200 nm. These **assemblies** were composed of two or more **filaments**, each 3-3.5 nm in diameter, and had the appearance of narrow ribbons. These types of structures also formed during the fibrillogenesis of Abeta and of the islet **amyloid** polypeptide (IAPP), however the rope-like, bifilar structures often seen in fibrils of Abeta and IAPP were not observed in alphata1 fibrils. In common with the fibrillogenesis of Abeta and IAPP, alphata1 fibril **assembly** involved an alpha-helix-fwdarwbeta-sheet conformational change and the development of Congo red binding capacity. The shared morphologic, spectroscopic, and tinctorial properties of alphata1, Abeta, and IAPP fibrils suggested that alphata1 fibrils might also share cytotoxic activity. However, alphata1 fibrils were not toxic to cultured rat primary cortical neurons or to PC12 cells. These results suggest that the potential to form fibrils is not limited to those proteins associated with amyloidoses and that fibril formation alone is not predictive of cytotoxic activity.

L58 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1999:164136 CAPLUS

DOCUMENT NUMBER: 130:322093

TITLE: Prion domain initiation of **amyloid** formation
in vitro from native Ure2p

AUTHOR(S): Taylor, Kimberly L.; Cheng, Naiqian; Williams, Robert
W.; Steven, Alasdair C.; Wickner, Reed B.

CORPORATE SOURCE: Laboratory of Biochemistry and Genetics, National
Institute of Diabetes and Digestive and Kidney
Diseases, National Institutes of Health, Bethesda, MD,
20892-0830, USA

SOURCE: Science (Washington, D. C.) (1999), 283(5406),
1339-1343
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The [URE3] non-Mendelian genetic element of *Saccharomyces cerevisiae* is an
infectious protein (prion) form of Ure2p, a regulator of nitrogen
catabolism. Here, synthetic Ure2p1-65 were shown to polymerize to form
filaments 40 to 45 angstroms in **diam.** with more than 60
% β sheet. Ure2p1-65 specifically induced full- **length**
native Ure2p to copolymerize under conditions where native Ure2p alone did
not polymerize. Like Ure2p in exts. of [URE3] strains, these 180- to
220-angstrom-**diam. filaments** were protease resistant.
The Ure2p1-65-Ure2p cofilaments could seed polymerization of native Ure2p to
form
thicker, less regular **filaments**. All **filaments**
stained with Congo Red to produce the green birefringence typical of
amyloid. This self-propagating **amyloid** formation can
explain the properties of [URE3].

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 97327024 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9183822

TITLE: As you like it.

AUTHOR: Ghadially F N

CORPORATE SOURCE: Department of Laboratory Medicine, Ottawa Civic Hospital,
Ontario, Canada.

SOURCE: Ultrastructural pathology, (1997 May-Jun) 21 (3) 211-26.
Ref: 38
Journal code: 8002867. ISSN: 0191-3123.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19990129
Entered Medline: 19970724

AB I have developed something of a reputation for criticizing freely and
frequently at our meetings and in my writings. You say you like this and
find it useful and entertaining. As you like it, you are welcome to more
of it. My comments and criticisms are presented under the following
headings: (1) criticize at your peril; (2) how it all started (unjustly
accused!); (3) abbreviations (a source of perennial aggravation,
confusion, and waste of time); (4) mysterious bodies in mesotheliomas; (5)
call a crystal a "crystal," not a "crystalloid"; (6) electron microscopy-a
study of osmium artifacts; (7) **length-to-diameter**
ratio of microvilli (mission impossible); (8) lamellar bodies (a popular

but debased term); (9) **amyloid filaments**, not fibers; (10) **filaments** and microtubules do not branch; (11) there is no such thing as pseudomelanosis; (12) botched histochemistry (just about every gastrointestinal tract pigment was misdiagnosed by histochemistry); (13) intranuclear Russell bodies, not "Dutcher bodies"; and (14) nuclear pores and virus-like particles (a new development in an old farce).

L58 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1991:245425 CAPLUS

DOCUMENT NUMBER: 114:245425

TITLE: Morphology and antibody recognition of synthetic β - **amyloid** peptides

AUTHOR(S): Fraser, P. E.; Duffy, L. K.; O'Malley, M. B.; Nguyen, J.; Inouye, H.; Kirschner, D. A.

CORPORATE SOURCE: Neurol. Res., Child. Hosp., Boston, MA, 02115, USA

SOURCE: Journal of Neuroscience Research (1991), 28(4), 474-85
CODEN: JNREDK; ISSN: 0360-4012

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β - **amyloid** protein (β -AP), this study investigated the ability of peptides sharing sequences with β -AP to form fibrils in vitro and to recognize anti- β - **amyloid** antisera. The peptides, which were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β -AP. Electron microscopy of neg.-stained or thin-sectioned preps. revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diams.** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diams.** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diam.** When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross- β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β -(1-28) was highly reactive in an inhibition-ELISA assay to β -(6-25) and β -(1-38), but not to β -(22-35), and immunostained β -(1-40) on Western blots. These studies show that the β -(6-25), β -(1-38) and β -(1-40) peptides can assemble into cross- β fibrils that retain epitopes characteristic of AD **amyloid**.

L58 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:405318 CAPLUS

DOCUMENT NUMBER: 111:5318

TITLE: Comparison of **amyloid** from Alzheimer's disease with synthetic peptide

AUTHOR(S): Duffy, Lawrence K.; Kirschner, Daniel A.; Joachim, Catharine L.; Sinclair, Alison; Inouye, Hideyo; Selkoe, Dennis J.

CORPORATE SOURCE: Cent. Neurol. dis., Brigham and Women's Hosp., Boston, MA, USA

SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988), Meeting Date 1987, 604-7. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.

CODEN: 56MDA6

DOCUMENT TYPE:

Conference

LANGUAGE:

English

AB X-ray patterns from partially dried, oriented pellets of β -peptide show characteristic cross β -spacings: a strong meridional arc at 4.76 Å and a diffuse equatorial arc at 10.6 Å. These spacings and the other ones observed at wide angles are similar to those reported for β -keratin. The series of small angle intensity maximum along the equator indicate the fibril is tubular with a **diam.** of 71 Å and that the wall is composed of 2 or 3 cross β -pleated sheets. When the synthetic β -peptide **length** was increased to 45 amino acids to encompass some of the proposed membrane spanning region, it became very insol. and 88% formic acid had to be used initially to solubilize it. X-ray patterns from this peptide (β -45) in the presence of 25% trifluoroacetic acid showed β -pleated sheet spacings at about 11 Å and 4.7 Å spacings; similar but weaker patterns have been recorded for cerebral vascular **amyloid**. An analog peptide, β -28 (16-Ala) was synthesized and produced polymorphic structures whose **assemblies** were 5 or 6 β -sheets instead of 2 or 3. There was a differential inhibition loss of 20% of binding of antibody to β -28-coated plates with β -28 (16-Ala) suggesting that Lys-16 is exposed in the **amyloid** fibrils and that alanine at that position promotes intersheet stacking. Thus, the Alzheimer's disease **amyloid** behavior can be examined using synthetic peptides. A preliminary model of an **amyloid** peptide fibril is presented. Further studies using peptide analogs can be used to test this model.

L58 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1988:201098 CAPLUS

DOCUMENT NUMBER: 108:201098

TITLE: A close ultrastructural relationship between sulfated proteoglycans and AA **amyloid** fibrils

AUTHOR(S): Snow, Alan David; Willmer, Jonathan; Kisilevsky, Robert

CORPORATE SOURCE: Dep. Pathol., Queen's Univ., Kingston, ON, Can.

SOURCE: Laboratory Investigation (1987), 57(6), 687-98

CODEN: LAINAW; ISSN: 0023-6837

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two cationic reagents, ruthenium red (RR) and cuproline blue (CB), were used to assess the morphol. and structural relationship between sulfated proteoglycans and AA **amyloid** fibrils in amyloidotic spleen and liver, and in isolated fibril prepns. Amyloidotic tissue fixed in the presence of RR showed RR granules, measuring 15 to 25 nm in **diam** .., over areas of electron-dense fibrils. In isolated fibril prepns., RR granules were specifically localized on **amyloid** fibrils. Amyloidotic tissue fixed in the presence of CB at 0.1M and 0.7M MgCl₂ showed both granule and filamentous (50 to 90 nm in **length**) staining only over areas of **amyloid** fibrils. This same staining localization was also seen in isolated fibril prepns. The RR and CB granules and **filaments**, are believed to represent proteoglycan monomers with the glycosaminoglycan chains collapsed onto the protein core. The persistent CB staining at 0.7M MgCl₂ suggested that highly sulfated proteoglycans were present. The glycosaminoglycan moiety has previously been identified as heparin/heparan sulfate. The intimate structural relationship between sulfated proteoglycans and AA **amyloid** fibrils, both in situ and in isolated fibril prepns., further suggests that these highly neg. charged mols. may have an important role in the pathogenesis of amyloidosis. Several pathogenetic scenarios are suggested.

L58 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1987:134807 CAPLUS

DOCUMENT NUMBER: 106:134807

TITLE: On the biology of prions
AUTHOR(S): Prusiner, S. B.; Gabizon, R.; McKinley, M. P.
CORPORATE SOURCE: Dep. Neurol., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Acta Neuropathologica (1987), 72(4), 299-314
CODEN: ANPTAL; ISSN: 0001-6322
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 147 refs. Prions cause scrapie and Creutzfeldt-Jakob disease (CJD); these infectious pathogens are composed largely, if not entirely, of protein mols. No prion-specific polynucleotide has been identified. Purified preps. of scrapie prions contain high titers (≥ 109.5 ID₅₀/mL), one protein (PrP 27-30), and **amyloid** rods (10-20 nm in diam. + 100-200 nm in length). Considerable evidence indicates that PrP 27-30 is required for and inseparable from scrapie infectivity. PrP 27-30 is encoded by a cellular gene and is derived from a larger protein, denoted PrPSc or PrP 33-35Sc, by protease digestion. A cellular isoform, designated PrPC or PprP 33-35C, is encoded by the same gene as PrPSc, and both proteins appear to be translated from the same 2.1 kb mRNA. Monoclonal antibodies to PrP 27-30, as well as antisera to PrP synthetic peptides, specifically react with both PrPC and PrPSc, establishing their relatedness. PrPC is digested by proteinase K, while PrPSc is converted to PrP 27-30 under the same conditions. Prion proteins are synthesized with signal peptides and are integrated into membranes. Detergent extraction of microsomal membranes isolated from scrapie-infected hamster brains solubilizes PrPC but induces PrPSc to polymerize into **amyloid** rods. This procedure allows separation of the two prion protein isoforms and the demonstration that PrPSc accumulates during scrapie infection, while the level of PrPC does not change. The prion **amyloid** rods generated by detergent extraction are identical morphol., except for length, to extracellular collections of prion **amyloid filaments** which form plaques in scrapie- and CJD-infected brains. The prion **amyloid** plaques stain with antibodies to PrP 27-30 and PrP peptides. PrP 33-35C does not accumulate in the extracellular space. Prion rods composed of PrP 27-30 can be dissociated into phospholipid vesicles with full retention of scrapie infectivity. The murine PrP gene (Prn-p) is linked to the Prn-i gene which controls the length of the scrapie incubation period. Prolonged incubation times are a cardinal feature of scrapie and CJD. While the central role of PrPSc in scrapie pathogenesis is well established, the chemical as well as conformational differences between PrPC and PrPSc are unknown but probably arise from post-translational modifications.

L58 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN DUPLICATE 9

ACCESSION NUMBER: 1985:380799 BIOSIS
DOCUMENT NUMBER: PREV198580050791; BA80:50791
TITLE: IDENTIFICATION OF PRION **AMYLOID FILAMENTS**
IN SCRAPIE-INFECTED BRAIN.
AUTHOR(S): DEARMOND S J [Reprint author]; MCKINLEY M P; BARRY R A;
BRAUNFELD M B; MCCOLLOCH J R; PRUSINER S B
CORPORATE SOURCE: DEP OF PATHOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO,
CALIF 94143, USA
SOURCE: Cell, (1985) Vol. 41, No. 1, pp. 221-236.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Extracellular collections of abnormal **filaments** composed of prion proteins were identified in the brains of scrapie-infected hamsters using immunoelectron microscopy. Some of the **filaments** were 1500 nm in length; generally, they exhibited a uniform diameter of 16 nm. Rarely, the **filaments** had a twisted

appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, as determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1641cxc

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 01 New pricing for the Save Answers for SciFinder Wizard within
STN Express with Discover!
NEWS 4 OCT 28 KOREAPAT now available on STN
NEWS 5 NOV 18 Current-awareness alerts, saved answer sets, and current
search transcripts to be affected by CERAB, COMPUAB, ELCOM,
and SOLIDSTATE reloads
NEWS 6 NOV 30 PHAR reloaded with additional data
NEWS 7 DEC 01 LISA now available on STN
NEWS 8 DEC 09 12 databases to be removed from STN on December 31, 2004
NEWS 9 DEC 15 MEDLINE update schedule for December 2004

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:18:48 ON 16 DEC 2004

=> file .meeting

'EVENTLINE' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available. If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE):ignore

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.42	0.42

FULL ESTIMATED COST

FILE 'AGRICOLA' ENTERED AT 15:19:39 ON 16 DEC 2004

FILE 'BIOTECHNO' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CONFSCI' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'HEALSAFE' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'IMSDRUGCONF' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (C) 2004 IMSWORLD Publications Ltd.

FILE 'LIFESCI' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'MEDICONF' ENTERED AT 15:19:39 ON 16 DEC 2004
COPYRIGHT (c) 2004 FAIRBASE Datenbank GmbH, Hannover, Germany

FILE 'PASCAL' ENTERED AT 15:19:39 ON 16 DEC 2004
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2004 INIST-CNRS. All rights reserved.

=> (cag repeat) and aggregate and length and diameter

L1	0 FILE AGRICOLA
L2	0 FILE BIOTECHNO
L3	0 FILE CONFSCI
L4	0 FILE HEALSAFE
L5	0 FILE IMSDRUGCONF
L6	0 FILE LIFESCI
L7	0 FILE MEDICONF
L8	0 FILE PASCAL

TOTAL FOR ALL FILES

L9	0 (CAG REPEAT) AND AGGREGATE AND LENGTH AND DIAMETER
----	--

=> file .chemistry
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
6.83	7.25

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 15:20:24 ON 16 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOTECHNO' ENTERED AT 15:20:24 ON 16 DEC 2004
COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'COMPENDEX' ENTERED AT 15:20:24 ON 16 DEC 2004
Compendex Compilation and Indexing (C) 2004
Elsevier Engineering Information Inc (EEI). All rights reserved.
Compendex (R) is a registered Trademark of Elsevier Engineering Information Inc.

FILE 'ANABSTR' ENTERED AT 15:20:24 ON 16 DEC 2004
COPYRIGHT (c) 2004 THE ROYAL SOCIETY OF CHEMISTRY (RSC)

FILE 'CERAB' ENTERED AT 15:20:24 ON 16 DEC 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'METADEX' ENTERED AT 15:20:24 ON 16 DEC 2004

COPYRIGHT (c) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'USPATFULL' ENTERED AT 15:20:24 ON 16 DEC 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> (cag repeat) and aggregate and length and diameter

L10	0	FILE CAPLUS
L11	0	FILE BIOTECHNO
L12	0	FILE COMPENDEX
L13	0	FILE ANABSTR
L14	0	FILE CERAB
L15	0	FILE METADEX
L16	0	FILE USPATFULL

TOTAL FOR ALL FILES

L17	0	(CAG REPEAT) AND AGGREGATE AND LENGTH AND DIAMETER
-----	---	--

=> glutamine and aggregate and length and diameter

L18	0	FILE CAPLUS
L19	0	FILE BIOTECHNO
L20	0	FILE COMPENDEX
L21	0	FILE ANABSTR
L22	0	FILE CERAB
L23	0	FILE METADEX
L24	1	FILE USPATFULL

TOTAL FOR ALL FILES

L25	1	GLUTAMINE AND AGGREGATE AND LENGTH AND DIAMETER
-----	---	---

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregate or assembly) and length

L26	2	FILE CAPLUS
L27	1	FILE BIOTECHNO
L28	0	FILE COMPENDEX
L29	0	FILE ANABSTR
L30	0	FILE CERAB
L31	0	FILE METADEX
L32	50	FILE USPATFULL

TOTAL FOR ALL FILES

L33	53	(CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH
-----	----	---

=> dup rem

ENTER L# LIST OR (END):126-127

PROCESSING COMPLETED FOR L26

PROCESSING COMPLETED FOR L27

L34	3	DUP REM L26-L27 (0 DUPLICATES REMOVED)
-----	---	--

=> d l34 ibib abs total

L34 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:716876 CAPLUS

DOCUMENT NUMBER: 139:287912

TITLE: **Ataxin-3** interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis

AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran

CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

SOURCE: Molecular and Cellular Biology (2003), 23(18),

6469-6483

CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin-3**. We investigated whether **ataxin-3** is a proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin-3** interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin-3** assoc. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin-3** is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:362711 CAPLUS

DOCUMENT NUMBER: 137:92006

TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics

AUTHOR(S): Chen, Songming; Berthelie, Valerie; Hamilton, J.

CORPORATE SOURCE: Bradley; O'Nuallain, Brian; Wetzel, Ronald
Graduate School of Medicine, University of Tennessee
Medical Center, Knoxville, TN, 37920, USA

SOURCE: Biochemistry (2002), 41(23), 7391-7399

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington's** disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β -sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied

here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the assembly process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington's** and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 3 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 1999:29124713 BIOTECHNO
 TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network
 AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
 CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
 E-mail: james.burke@duke.edu
 SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
 CODEN: EXNEAC ISSN: 0014-4886
 DOCUMENT TYPE: Journal; Article
 COUNTRY: United States
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO
 AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-length polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-length polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-length polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

=> file .meeting

'EVENTLINE' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files that are available. If you have requested multiple files, you can specify a corrected file name or you can enter "IGNORE" to continue accessing the remaining file names entered.

ENTER A FILE NAME OR (IGNORE):ignore

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
49.60	56.85

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION

CA SUBSCRIBER PRICE

-1.40

-1.40

FILE 'AGRICOLA' ENTERED AT 15:24:54 ON 16 DEC 2004

FILE 'BIOTECHNO' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CONFSCI' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'HEALSAFE' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'IMSDRUGCONF' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 IMSWORLD Publications Ltd.

FILE 'LIFESCI' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)

FILE 'MEDICONF' ENTERED AT 15:24:54 ON 16 DEC 2004

COPYRIGHT (c) 2004 FAIRBASE Datenbank GmbH, Hannover, Germany

FILE 'PASCAL' ENTERED AT 15:24:54 ON 16 DEC 2004

Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2004 INIST-CNRS. All rights reserved.

=> amyloid and (filament or aggregate or assembly) and length and diameter

L35	1 FILE AGRICOLA
L36	4 FILE BIOTECHNO
L37	0 FILE CONFSCI
L38	0 FILE HEALSAFE
L39	0 FILE IMSDRUGCONF
L40	3 FILE LIFESCI
L41	0 FILE MEDICONF
L42	1 FILE PASCAL

TOTAL FOR ALL FILES

L43	9 AMYLOID AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH AND DIAMETER
-----	---

=> dup rem

ENTER L# LIST OR (END):L43

DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE

PROCESSING COMPLETED FOR L43

L44	5 DUP REM L43 (4 DUPLICATES REMOVED)
-----	--------------------------------------

=> d l44 ibib abs total

L44 ANSWER 1 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2003:37345999 BIOTECHNO

TITLE: Architecture of Ure2p Prion **Filaments**: The
N-terminal domains form a central core fiber

AUTHOR: Baxa U.; Taylor K.L.; Wall J.S.; Simon M.N.; Cheng N.;
Wickner R.B.; Steven A.C.

CORPORATE SOURCE: A.C. Steven, Bldg. 50, MSC 8025, 50 South Dr.,
Bethesda, MD 20892-8025, United States.

SOURCE: E-mail: Alasdair_Steven@nih.gov

Journal of Biological Chemistry, (31 OCT 2003), 278/44
(43717-43727), 46 reference(s)

CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 2003:37345999 BIOTECHNO

AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p determines its in vivo prion properties and in vitro amyloid-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diameter Ure2p filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diameters** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning transmission electron microscopy (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

L44 ANSWER 2 OF 5 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved.
(2004) on STN DUPLICATE 1

ACCESSION NUMBER: 2002:50889 AGRICOLA

DOCUMENT NUMBER: IND23281705

TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein.

AUTHOR(S): Baxa, U.; Speransky, V.; Steven, A.C.; Wickner, R.B.

AVAILABILITY: DNAL (500 N21P)

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Apr 16, 2002. Vol. 99, No. 8. p. 5253-5260
Publisher: Washington, D.C. : National Academy of Sciences,
CODEN: PNASA6; ISSN: 0027-8424

NOTE: Includes references

PUB. COUNTRY: District of Columbia; United States

DOCUMENT TYPE: Article; Conference

FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension

LANGUAGE: English

AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diameters** increased with the mass of the appended enzyme. The

helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all beta-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

L44 ANSWER 3 OF 5 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 2
 ACCESSION NUMBER: 1999:39603 LIFESCI
 TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
 AUTHOR: Taylor, K.L.; Cheng, Naiqian; Williams, R.W.; Steven, A.C.; Wickner, R.B.*
 CORPORATE SOURCE: Lab. Biochem. and Genet., Natl. Inst. Health, Bethesda, MD 20892-0830, USA; E-mail: wickner@helix.nih.gov
 SOURCE: Science (Washington) [Science (Wash.)], (19990226) vol. 283, no. 5406, pp. 1339-1343. ISSN: 0036-8075.
 DOCUMENT TYPE: Journal
 FILE SEGMENT: K; V
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB The [URE3] non-Mendelian genetic element of *Saccharomyces cerevisiae* is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p super(1-65) were shown to polymerize to form **filaments** 40 to 45 angstroms in **diameter** with more than 60 percent beta sheet. Ure2p specifically induced full-**length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in extracts of [URE3] strains, these 180- to 220-angstrom-**diameter filaments** were protease resistant. The Ure2p super(1-65)-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular **filaments**. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].

L44 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
 ACCESSION NUMBER: 1991:21180842 BIOTECHNO
 TITLE: Morphology and antibody recognition of synthetic β - **amyloid** peptides
 AUTHOR: Fraser P.E.; Duffy L.K.; O'Malley M.B.; Nguyen J.; Inouye H.; Kirschner D.A.
 CORPORATE SOURCE: Neurology Research, Children's Hospital, Enders 2, 320 Longwood Ave., Boston, MA 02115, United States.
 SOURCE: Journal of Neuroscience Research, (1991), 28/4 (474-485)
 CODEN: JNREDK ISSN: 0360-4012
 DOCUMENT TYPE: Journal; Article
 COUNTRY: United States
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AN 1991:21180842 BIOTECHNO
 AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β -**amyloid** protein (β -AP), we investigated the ability of peptides sharing sequences with β -AP to form fibrils in vitro and to recognize anti- β - **amyloid** antisera. The peptides, which

were synthesized using a Fmoc solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full length of β -AP. Electron microscopy of negative-stained or thin-sectioned preparations revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diameters** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diameters** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1,100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diameter**. When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross- β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β -(1-28) was highly reactive in an inhibition-ELISA assay to β -(6-25) and β -(1-38), but not to β -(22-35), and immunostained β -(1-40) on Western blots. These studies show that the β -(6-25), β -(1-38) and β -(1-40) peptides can assemble into cross- β fibrils that retain epitopes characteristic of AD **amyloid**.

L44 ANSWER 5 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1985:15068440 BIOTECHNO
TITLE: Identification of prion **amyloid**
filaments in scrapie-infected brain
AUTHOR: DeArmond S.J.; McKinley M.P.; Barry R.A.; et al.
CORPORATE SOURCE: Department of Pathology, University of California, San
Francisco, CA 94143, United States.
SOURCE: Cell, (1985), 41/1 (221-235)
CODEN: CELLB5
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English

AN 1985:15068440 BIOTECHNO

AB Extracellular collections of abnormal **filaments** composed of prion proteins have been identified in the brains of scrapie-infected hamsters using immuno-electron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, and determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

=> file .jacob

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

19.73

76.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.40

FILE 'CAPLUS' ENTERED AT 15:31:45 ON 16 DEC 2004
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:31:45 ON 16 DEC 2004
 Copyright (c) 2004 The Thomson Corporation.

FILE 'MEDLINE' ENTERED AT 15:31:45 ON 16 DEC 2004

FILE 'EMBASE' ENTERED AT 15:31:45 ON 16 DEC 2004
 COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'USPATFULL' ENTERED AT 15:31:45 ON 16 DEC 2004
 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregate or assembly) and length

L45	2 FILE CAPLUS
L46	4 FILE BIOSIS
L47	1 FILE MEDLINE
L48	2 FILE EMBASE
L49	50 FILE USPATFULL

TOTAL FOR ALL FILES

L50	59 (CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH
-----	--

=> dup rem

ENTER L# LIST OR (END):145-148
 PROCESSING COMPLETED FOR L45
 PROCESSING COMPLETED FOR L46
 PROCESSING COMPLETED FOR L47
 PROCESSING COMPLETED FOR L48
 L51 5 DUP REM L45-L48 (4 DUPLICATES REMOVED)

=> d l51 ibib abs total

L51 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:716876 CAPLUS

DOCUMENT NUMBER: 139:287912

TITLE: **Ataxin-3** interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis
 AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran

CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

SOURCE: Molecular and Cellular Biology (2003), 23(18), 6469-6483

CODEN: MCEBD4; ISSN: 0270-7306

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin-3**. We investigated whether **ataxin-3** is a

proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin-3** interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin-3** assoc. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin-3** is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:278678 BIOSIS
DOCUMENT NUMBER: PREV200200278678
TITLE: Remedy for **CAG repeat** expansion diseases.
AUTHOR(S): Tsuji, Shoji [Inventor, Reprint author]
CORPORATE SOURCE: Niigata, Japan
ASSIGNEE: Niigata University, Japan
PATENT INFORMATION: US 6355690 March 12, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 12, 2002) Vol. 1256, No. 2.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB To elucidate the molecular mechanisms of "gain of toxic function" of expanded polyglutamine stretches in **CAG repeat** expansion diseases, the inventors established an expression system of full-**length** and truncated cDNAs for dentatorubral-pallidoluysian atrophy (**DRPLA**) and found that truncated **DRPLA** proteins containing the expanded polyglutamine stretch, but not the full-**length** protein, form peri- and intra-nuclear aggregates consisting of **filaments** and concomitant apoptosis. The apoptotic cell death was partially suppressed by transglutaminase inhibitors, cystamine and monodansyl cadaverine, raising the possibility of involvement of transglutaminase reaction. The results may provide a potential basis for the development of therapeutic measures for **CAG repeat** expansion diseases.

L51 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelmer, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzell, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the

cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington's** disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β -sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington's** and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
 ACCESSION NUMBER: 2001:433998 BIOSIS
 DOCUMENT NUMBER: PREV200100433998
 TITLE: A microtiter plate assay for polyglutamine aggregate extension.
 AUTHOR(S): Berthelie, Valerie; Hamilton, J. Bradley; Chen, Songming; Wetzel, Ronald [Reprint author]
 CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, R221, Knoxville, TN, 37920, USA
 SOURCE: Analytical Biochemistry, (August 15, 2001) Vol. 295, No. 2, pp. 227-236. print.
 CODEN: ANBCA2. ISSN: 0003-2697.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 12 Sep 2001
 Last Updated on STN: 22 Feb 2002

AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded **CAG repeat** disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln peptide. Europium-streptavidin complexation of the immobilized biotin,

followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the **assembly** mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln **length** dependence. The assay also will be a valuable tool for screening and characterizing anti-aggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism.

L51 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
DUPLICATE 2

ACCESSION NUMBER: 1999:180905 BIOSIS
DOCUMENT NUMBER: PREV199900180905
TITLE: Expanded polyglutamine domain proteins bind neurofilament
and alter the neurofilament network.
AUTHOR(S): Nagai, Yoshitaka; Onodera, Osamu; Chun, Jerold;
Strittmatter, Warren J.; Burke, James R. [Reprint author]
CORPORATE SOURCE: Department of Medicine (Neurology), Duke University Medical
Center, Durham, NC, 27710, USA
SOURCE: Experimental Neurology, (Feb., 1999) Vol. 155, No. 2, pp.
195-203. print.
CODEN: EXNEAC. ISSN: 0014-4886.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

AB Eight inherited neurodegenerative diseases are caused by genes with
expanded **CAG repeats** coding for polyglutamine domains
in the disease-producing proteins. The mechanism by which this expanded
polyglutamine domain causes neurodegenerative disease is unknown, but
nuclear and cytoplasmic polyglutamine protein aggregation is a common
feature. In transfected COS7 cells, expanded polyglutamine proteins
aggregate and disrupt the vimentin intermediate **filament**
network. Since neurons have an intermediate **filament** network
composed of neurofilament (NF) and NF abnormalities occur in
neurodegenerative diseases, we examined whether pathologic-**length**
polyglutamine domain proteins also interact with NF. We expressed varying
lengths polyglutamine-green fluorescent protein fusion proteins in
a neuroblast cell line, TR1. Pathologic-**length**
polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates
surrounded by neurofilament. Immunoprecipitation of pathologic-**length**
polyglutamine proteins coisolated 68-kDa NF protein demonstrating
molecular interaction. These observations suggest that polyglutamine
interaction with NF is important in the pathogenesis of the polyglutamine
repeat diseases.

=> amyloid and (filament or aggregate or assembly) and length and diameter

L52 11 FILE CAPLUS
L53 8 FILE BIOSIS
L54 9 FILE MEDLINE
L55 10 FILE EMBASE
L56 793 FILE USPATFULL

TOTAL FOR ALL FILES

L57 831 AMYLOID AND (FILAMENT OR AGGREGATE OR ASSEMBLY) AND LENGTH AND
DIAMETER

=> dup rem

ENTER L# LIST OR (END):152-155

PROCESSING COMPLETED FOR L52

PROCESSING COMPLETED FOR L53

PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L55
L58 16 DUP REM L52-L55 (22 DUPLICATES REMOVED)

=> d l58 ibib abs total

L58 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:495393 CAPLUS

DOCUMENT NUMBER: 141:201912

TITLE: The formation of straight and twisted
filaments from short tau peptides

AUTHOR(S): Goux, Warren J.; Kopplin, Lauren; Nguyen, Anh D.;
Leak, Kathryn; Rutkofsky, Marni; Shanmuganandam,
Vasanthi D.; Sharma, Deepak; Inouye, Hideyo;
Kirschner, Daniel A.

CORPORATE SOURCE: Department of Chemistry, the University of Texas at
Dallas, Richardson, TX, 75083-0688, USA

SOURCE: Journal of Biological Chemistry (2004), 279(26),
26868-26875

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We studied fibril formation in a family of peptides based on PHF6
(VQIVYK), a short peptide segment found in the microtubule binding region
of tau protein. N-Acetylated peptides AcVYK-amide (AcVYK), AcIVYK-amide
(AcPHF4), AcQIVYK-amide (AcPHF5), and AcV-QIVYK-amide (AcPHF6) rapidly
formed straight **filaments** in the presence of 0.15 M NaCl, each
composed of two laterally aligned protofilaments .apprx.5 nm in width.
X-ray fiber diffraction showed the omnipresent sharp 4.7-Å reflection
indicating that the scattering objects are likely elongated along the
hydrogen-bonding direction in a cross-β conformation, and Fourier
transform IR suggested the peptide chains were in a parallel (AcVYK,
AcPHF6) or antiparallel (AcPHF4, AcPHF5) β-sheet configuration. The
dipeptide N-acetyl-YK-amide (AcYK) formed globular structures .apprx.200
nm to 1 μm in **diam**. The polymerization rate, as measured by
thioflavin S binding, increased with the **length** of the peptide
going from AcYK → AcPHF6, and peptides that aggregated most rapidly
displayed CD spectra consistent with β-sheet structure. There was a
3-fold decrease in rate when Val was substituted for Ile or Gln, nearly a
10-fold decrease when Ala was substituted for Tyr, and an increase in
polymerization rate when Glu was substituted for Lys. Twisted **filaments**
, composed of four laterally aligned protofilaments (9-19 nm width,
.apprx.90 nm half-periodicity), were formed by mixing AcPHF6 with AcVYK.
Taken together these results suggest that the core of PHF6 is localized at
VYK, and the interaction between small amphiphilic segments of tau may
initiate nucleation and lead to **filaments** displaying paired
helical **filament** morphol.

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
STN

ACCESSION NUMBER: 2004:160995 BIOSIS

DOCUMENT NUMBER: PREV200400164922

TITLE: Formation of amyloid from superoxide dismutase.

AUTHOR(S): Oztug, Zeynep [Reprint Author]; Padua, Shelby [Reprint
Author]; Downes, Sean [Reprint Author]; Cohlberg, Jeffrey
A. [Reprint Author]; Rodriguez, Jorge; Doucette, Peter;
Valentine, Joan S.

CORPORATE SOURCE: Dept of Chemistry and Biochemistry, California State
University, Long Beach, Long Beach, CA, USA

SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

504a. print.

Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004.

Biophysical Society.

ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 24 Mar 2004

Last Updated on STN: 24 Mar 2004

AB Mutations in copper-zinc superoxide dismutase (SOD) are the cause of 20 percent of the cases of familial amyotrophic lateral sclerosis (FALS). Insoluble deposits containing SOD are found in motor neurons of FALS patients, some of which are reactive with the **amyloid**-specific dye thioflavin S. It has been proposed that the mutations cause the disease by increasing the tendency of SOD to aggregate. Furthermore, certain SOD crystal structures show linear arrays of SOD dimers similar to **amyloid filaments**. Therefore, conditions were sought under which SOD forms **amyloid**. Protein solutions were agitated at 37C in the presence of thioflavin T, and **amyloid** formation was detected by monitoring fluorescence with a microplate reader. Wild-type SOD formed **amyloid** at pH 3 and 0.5-2 M guanidine hydrochloride, with an optimum of about 1 M guanidine. The kinetics showed a lag phase of variable length, typically about 24 hr, followed by a rise in fluorescence over a period of a few hours. Incubation of the product with Congo Red produced a shift in the absorbance peak from 510 nm to 542 nm. Transmission electron microscopy revealed straight **filaments** with **diameters** of about 10 nm, often appearing as bundles up to 50 nm in **diameter**. Apo-SOD did not form **amyloid** under these conditions. Various FALS-related mutant SODs also formed **amyloid filaments** at acidic pH and low concentrations of guanidine. For some of the mutants less acidic conditions were required to promote **amyloid** formation. Under some conditions, mutant SODs formed **amyloid** only when seeded by preexisting **amyloid**, while seeding appeared to have no effect with other samples. 30% acetonitrile can substitute for guanidine hydrochloride in promoting **amyloid** formation. The results may be relevant to the aggregation of SOD which occurs in motor neurons in FALS.

L58 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:660806 CAPLUS

TITLE: Nanostructure of β -sheet fibrils constructed by unfolded β -hairpin peptide self- **assembly**

AUTHOR(S): Lamm, Matthew S.; Rajagopal, Karthikan; Schneider, Joel P.; Pochan, Darrin J.

CORPORATE SOURCE: Department of Materials Science and Engineering, University of Delaware, Newark, DE, 19716, USA

SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), POLY-345. American Chemical Society: Washington, D. C.

CODEN: 69FTZ8

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB A 20-residue peptide consisting of alternating valine and lysine residues flanking a tripeptide turn sequence has been shown to self-assemble via differing pathways into dramatically different materials, depending on the primary structure of the turn sequence. Under appropriate solution conditions, peptides with type II' turn sequences intramolecularly fold leading to β -sheet rich, reversible hydrogelation. Alternatively, almost identical peptides, differing only in turn sequence that strongly disfavors intramol. folding, adopt an extended β -sheet conformation and irreversibly assemble into β - **amyloid**-like, prion-like

fibrillar structures. The resulting fibrillar structures are analyzed using transmission electron microscopy, atomic force microscopy and x-ray diffraction; an untwisted, un-branched morphol. is observed characterized by lateral **assembly** of .apprx.2.5nm **diam.** **filaments** and up to microns in **length.** Lateral association of **filaments** produced fibril widths of 100nm or more. Each fibril has an exact height of .apprx.6.7nm suggesting that each peptide is in an extended conformation with the peptide backbone orthogonal to both the fibril axis and the direction of lamination.

L58 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:850847 CAPLUS
DOCUMENT NUMBER: 140:2085
TITLE: Architecture of Ure2p Prion **Filaments**: the N-terminal domains form a central core fiber
AUTHOR(S): Baxa, Ulrich; Taylor, Kimberly L.; Wall, Joseph S.; Simon, Martha N.; Cheng, Naiqian; Wickner, Reed B.; Steven, Alasdair C.
CORPORATE SOURCE: Lab. Struct. Biol., Natl. Inst. Arthritis, Musculoskeletal, and Skin Dis., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Biological Chemistry (2003), 278(44), 43717-43727
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p **dets.** its in vivo prion properties and in vitro **amyloid-forming** ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diam.** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diam.** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning TEM (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:72748 CAPLUS
DOCUMENT NUMBER: 136:146104
TITLE: Human stress genes identified using DNA microarrays
INVENTOR(S): Chenchik, Alex; Lukashev, Matvey E.
PATENT ASSIGNEE(S): Clontech, USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 441,920.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002009730	A1	20020124	US 2001-782909	20010213
PRIORITY APPLN. INFO.:			US 1998-222256	B2 19981228
			US 1999-440305	B2 19991117
			US 1999-441920	A2 19991117

AB Human stress arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe composition of unique polynucleotides corresponding to a human stress gene. The average **length** of the polynucleotide probes is between 50 to 1000 nucleotides. The d. of the spots on the array did not exceed 400/cm2 and the spots had a **diam** . ranging between 10 to 5000 μ m. Furthermore, the number of polynucleotide probe spots on the array ranged between 50 to 2000 nucleotides. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of human stress genes. 236 Different human stress genes were identified using this approach.

L58 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:316601 CAPLUS

DOCUMENT NUMBER: 137:45099

TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein

AUTHOR(S): Baxa, Ulrich; Speransky, Vladislav; Steven, Alasdair C.; Wickner, Reed B.

CORPORATE SOURCE: Laboratories of Structural Biology, National Institute of Arthritis, Musculoskeletal Diseases, and Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(8), 5253-5260
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich N-terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diam**s . increased with the mass of the appended enzyme. The helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all β -sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:703452 CAPLUS
DOCUMENT NUMBER: 138:2785
TITLE: Examining the structure of the mature amyloid fibril
AUTHOR(S): Makin, O. S.; Serpell, L. C.
CORPORATE SOURCE: Structural Medicine Unit, Cambridge Institute for Medical Research, Cambridge, CB2 2XY, UK
SOURCE: Biochemical Society Transactions (2002), 30(4), 521-525
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The pathogenesis of the group of diseases known collectively as the amyloidoses is characterized by the deposition of insol. amyloid fibrils. These are straight, unbranching structures about 70-120 Å (1 Å = 0.1 nm) in diam. and of indeterminate length formed by the self-assembly of a diverse group of normally soluble proteins. Knowledge of the structure of these fibrils is necessary for the understanding of their abnormal assembly and deposition, possibly leading to the rational design of therapeutic agents for their prevention or disaggregation. Structural elucidation is impeded by fibril insol. and inability to crystallize, thus preventing the use of x-ray crystallog. and solution NMR. CD, Fourier-transform IR spectroscopy and light scattering have been used in the study of the mechanism of fibril formation. This review concs. on the structural information about the final, mature fibril and in particular the complementary techniques of cryo-electron microscopy, solid-state NMR and x-ray fiber diffraction.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001241576 EMBASE
TITLE: Yeast prions act as genes composed of self-propagating protein amyloids.
AUTHOR: Wickner R.B.; Taylor K.L.; Edskes H.K.; Maddelein M.-L.; Moriyama H.; Tibor Roberts B.
CORPORATE SOURCE: R.B. Wickner, Laboratory of Biochemistry, Natl. Inst. Diab. Digest./Kid. Dis., National Institutes of Health, Bethesda, MD 20892, United States
SOURCE: Advances in Protein Chemistry, (2001) 57/- (313-334).
Refs: 71
ISSN: 0065-3233 CODEN: APCHA2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We proposed genetic properties by which prions can be recognized among infectious elements. This indicated that [URE3] and [PSI], two nonchromosomal genetic elements of yeast, were prions (infectious altered forms) of Ure2p and Sup35p, respectively. Overexpression of Ure2p leads to the de novo appearance of the [URE3] prion, and the N-terminal 65-80 residues (the prion domain) are specifically responsible for this prion-inducing activity. The prion domain is sufficient to propagate [URE3] and is necessary for a Ure2p molecule to be affected by [URE3]. The remaining C-terminal residues 81-354 are responsible for nitrogen catabolite repression, the normal function of Ure2p. Ure2p is protease-resistant specifically in extracts of [URE3] strains and is

aggregated in vivo specifically in such strains. The chemically synthesized Ure2p prion domain (Ure2p(1-65)) spontaneously forms classic **amyloid filaments** (50 A diameter) in vitro, and specifically induces the native full length Ure2p to form a 1:1 **amyloid** cofilament (200 A). These **amyloid** cofilaments can prime amyloid filament formation by an excess of native Ure2p. The features of the in vitro **amyloid** propagation reaction appear to reproduce the in vivo properties of [URE3] prion propagation. This system may be useful for detecting new prions, finding **amyloid-inducing** and **amyloid-curing** agents, and determining the cellular components that affect the initiation and propagation of infectious amyloids. The [Het-s] prion was found in the filamentous fungus *Podospora anserina* by similar genetic tests to those we used for [URE3] and [PSI]. [Het-s] is necessary for a normal function of *Podospora* cells, heterokaryon incompatibility. This suggests that other normal cellular functions may involve a prion-like mechanism.

L58 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:80946 BIOSIS

DOCUMENT NUMBER: PREV200100080946

TITLE: A de novo designed helix-turn-helix peptide forms nontoxic **amyloid** fibrils.

AUTHOR(S): Fezoui, Y. [Reprint author]; Hartley, D. M.; Walsh, D. M.; Selkoe, D. J.; Osterhout, J. J.; Teplow, D. B.

CORPORATE SOURCE: Brigham and Women's Hospital, Boston, MA, USA

SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-299.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Feb 2001

Last Updated on STN: 12 Feb 2002

AB During fibrillogenesis studies of the **amyloid** beta-protein (Abeta), we sought a non-amyloidogenic "negative control" peptide. Prior work suggested that alphata, a de novo designed, monomeric, 38-residue alpha-helix-turn-alpha-helix peptide would be ideal. alphata was developed as a model for the study of protein folding intermediates and has a protein-like sequence and a stable tertiary structure. At pH 3.6 and pH 10.5, alphata showed no aggregation after 8 weeks of incubation at 37degreeC. Surprisingly, at neutral pH, alphata formed fibrils after 2 days of incubation at 37degreeC. Negative staining and electron microscopy revealed non-branching fibril **assemblies** 6-10 nm in width, which varied in length from 200 to 1200 nm. These **assemblies** were composed of two or more **filaments**, each 3-3.5 nm in **diameter**, and had the appearance of narrow ribbons. These types of structures also formed during the fibrillogenesis of Abeta and of the islet **amyloid** polypeptide (IAPP), however the rope-like, bifilar structures often seen in fibrils of Abeta and IAPP were not observed in alphata fibrils. In common with the fibrillogenesis of Abeta and IAPP, alphata fibril **assembly** involved an alpha-helixfwdarwbeta-sheet conformational change and the development of Congo red binding capacity. The shared morphologic, spectroscopic, and tinctorial properties of alphata, Abeta, and IAPP fibrils suggested that alphata fibrils might also share cytotoxic activity. However, alphata fibrils were not toxic to cultured rat primary cortical neurons or to PC12 cells. These results suggest that the potential to form fibrils is not limited to those proteins associated with amyloidosis and that fibril formation alone is not predictive of cytotoxic activity.

L58 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1999:164136 CAPLUS

DOCUMENT NUMBER: 130:322093

TITLE: Prion domain initiation of **amyloid** formation
in vitro from native Ure2p

AUTHOR(S): Taylor, Kimberly L.; Cheng, Naiqian; Williams, Robert
W.; Steven, Alasdair C.; Wickner, Reed B.

CORPORATE SOURCE: Laboratory of Biochemistry and Genetics, National
Institute of Diabetes and Digestive and Kidney
Diseases, National Institutes of Health, Bethesda, MD,
20892-0830, USA

SOURCE: Science (Washington, D. C.) (1999), 283(5406),
1339-1343

CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The [URE3] non-Mendelian genetic element of *Saccharomyces cerevisiae* is an
infectious protein (prion) form of Ure2p, a regulator of nitrogen
catabolism. Here, synthetic Ure2p1-65 were shown to polymerize to form
filaments 40 to 45 angstroms in **diam.** with more than 60
% β sheet. Ure2p1-65 specifically induced full- **length**
native Ure2p to copolymerize under conditions where native Ure2p alone did
not polymerize. Like Ure2p in exts. of [URE3] strains, these 180- to
220-angstrom-**diam. filaments** were protease resistant.
The Ure2p1-65-Ure2p cofilaments could seed polymerization of native Ure2p to
form
thicker, less regular filaments. All **filaments**
stained with Congo Red to produce the green birefringence typical of
amyloid. This self-propagating **amyloid** formation can
explain the properties of [URE3].

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 97327024 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9183822

TITLE: As you like it.

AUTHOR: Ghadially F N

CORPORATE SOURCE: Department of Laboratory Medicine, Ottawa Civic Hospital,
Ontario, Canada.

SOURCE: Ultrastructural pathology, (1997 May-Jun) 21 (3) 211-26.
Ref: 38

Journal code: 8002867. ISSN: 0191-3123.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199707

ENTRY DATE: Entered STN: 19970805

Last Updated on STN: 19990129

Entered Medline: 19970724

AB I have developed something of a reputation for criticizing freely and
frequently at our meetings and in my writings. You say you like this and
find it useful and entertaining. As you like it, you are welcome to more
of it. My comments and criticisms are presented under the following
headings: (1) criticize at your peril; (2) how it all started (unjustly
accused!); (3) abbreviations (a source of perennial aggravation,
confusion, and waste of time); (4) mysterious bodies in mesotheliomas; (5)
call a crystal a "crystal," not a "crystalloid"; (6) electron microscopy-a
study of osmium artifacts; (7) **length-to-diameter**
ratio of microvilli (mission impossible); (8) lamellar bodies (a popular

but debased term); (9) **amyloid filaments**, not fibers; (10) **filaments** and microtubules do not branch; (11) there is no such thing as pseudomelanosis; (12) botched histochemistry (just about every gastrointestinal tract pigment was misdiagnosed by histochemistry); (13) intranuclear Russell bodies, not "Dutcher bodies"; and (14) nuclear pores and virus-like particles (a new development in an old farce).

L58 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1991:245425 CAPLUS
DOCUMENT NUMBER: 114:245425
TITLE: Morphology and antibody recognition of synthetic β - **amyloid** peptides
AUTHOR(S): Fraser, P. E.; Duffy, L. K.; O'Malley, M. B.; Nguyen, J.; Inouye, H.; Kirschner, D. A.
CORPORATE SOURCE: Neurol. Res., Child. Hosp., Boston, MA, 02115, USA
SOURCE: Journal of Neuroscience Research (1991), 28(4), 474-85
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β -**amyloid** protein (β -AP), this study investigated the ability of peptides sharing sequences with β -AP to form fibrils in vitro and to recognize anti- β - **amyloid** antisera. The peptides, which were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β -AP. Electron microscopy of neg.-stained or thin-sectioned preps. revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diams.** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diams.** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diam.** When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross- β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β -(1-28) was highly reactive in an inhibition-ELISA assay to β -(6-25) and β -(1-38), but not to β -(22-35), and immunostained β -(1-40) on Western blots. These studies show that the β -(6-25), β -(1-38) and β -(1-40) peptides can assemble into cross- β fibrils that retain epitopes characteristic of AD **amyloid**.

L58 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:405318 CAPLUS
DOCUMENT NUMBER: 111:5318
TITLE: Comparison of **amyloid** from Alzheimer's disease with synthetic peptide
AUTHOR(S): Duffy, Lawrence K.; Kirschner, Daniel A.; Joachim, Catharine L.; Sinclair, Alison; Inouye, Hideyo; Selkoe, Dennis J.
CORPORATE SOURCE: Cent. Neurol. dis., Brigham and Women's Hosp., Boston, MA, USA
SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988), Meeting Date 1987, 604-7. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.

CODEN: 56MDA6

DOCUMENT TYPE:

Conference

LANGUAGE:

English

AB X-ray patterns from partially dried, oriented pellets of β -peptide show characteristic cross β -spacings: a strong meriodional arc at 4.76 Å and a diffuse equatorial arc at 10.6 Å. These spacings and the other ones observed at wide angles are similar to those reported for β -keratin. The series of small angle intensity maximum along the equator indicate the fibril is tubular with a **diam.** of 71 Å and that the wall is composed of 2 or 3 cross β -pleated sheets. When the synthetic β -peptide length was increased to 45 amino acids to encompass some of the proposed membrane spanning region, it became very insol. and 88% formic acid had to be used initially to solubilize it. X-ray patterns from this peptide (β -45) in the presence of 25% trifluoroacetic acid showed β -pleated sheet spacings at about 11 Å and 4.7 Å spacings; similar but weaker patterns have been recorded for cerebral vascular **amyloid**. An analog peptide, β -28 (16-Ala) was synthesized and produced polymorphic structures whose **assemblies** were 5 or 6 β -sheets instead of 2 or 3. There was a differential inhibition loss of 20% of binding of antibody to β -28-coated plates with β -28 (16-Ala) suggesting that Lys-16 is exposed in the **amyloid** fibrils and that alanine at that position promotes intersheet stacking. Thus, the Alzheimer's disease **amyloid** behavior can be examined using synthetic peptides. A preliminary model of an **amyloid** peptide fibril is presented. Further studies using peptide analogs can be used to test this model.

L58 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1988:201098 CAPLUS

DOCUMENT NUMBER: 108:201098

TITLE: A close ultrastructural relationship between sulfated proteoglycans and AA **amyloid** fibrils

AUTHOR(S): Snow, Alan David; Willmer, Jonathan; Kisilevsky, Robert

CORPORATE SOURCE: Dep. Pathol., Queen's Univ., Kingston, ON, Can.

SOURCE: Laboratory Investigation (1987), 57(6), 687-98

CODEN: LAINAW; ISSN: 0023-6837

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two cationic reagents, ruthenium red (RR) and cuproinic blue (CB), were used to assess the morphol. and structural relationship between sulfated proteoglycans and AA **amyloid** fibrils in amyloidotic spleen and liver, and in isolated fibril prepns. Amyloidotic tissue fixed in the presence of RR showed RR granules, measuring 15 to 25 nm in **diam** .., over areas of electron-dense fibrils. In isolated fibril prepns., RR granules were specifically localized on **amyloid** fibrils. Amyloidotic tissue fixed in the presence of CB at 0.1M and 0.7M MgCl₂ showed both granule and filamentous (50 to 90 nm in **length**) staining only over areas of **amyloid** fibrils. This same staining localization was also seen in isolated fibril prepns. The RR and CB granules and **filaments**, are believed to represent proteoglycan monomers with the glycosaminoglycan chains collapsed onto the protein core. The persistent CB staining at 0.7M MgCl₂ suggested that highly sulfated proteoglycans were present. The glycosaminoglycan moiety has previously been identified as heparin/heparan sulfate. The intimate structural relationship between sulfated proteoglycans and AA **amyloid** fibrils, both in situ and in isolated fibril prepns., further suggests that these highly neg. charged mols. may have an important role in the pathogenesis of amyloidosis. Several pathogenetic scenarios are suggested.

L58 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1987:134807 CAPLUS

DOCUMENT NUMBER: 106:134807

TITLE: On the biology of prions
 AUTHOR(S): Prusiner, S. B.; Gabizon, R.; McKinley, M. P.
 CORPORATE SOURCE: Dep. Neurol., Univ. California, San Francisco, CA, 94143, USA
 SOURCE: Acta Neuropathologica (1987), 72(4), 299-314
 CODEN: ANPTAL; ISSN: 0001-6322
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 147 refs. Prions cause scrapie and Creutzfeldt-Jakob disease (CJD); these infectious pathogens are composed largely, if not entirely, of protein mols. No prion-specific polynucleotide has been identified. Purified preps. of scrapie prions contain high titers (≥ 109.5 ID₅₀/mL), one protein (PrP 27-30), and **amyloid** rods (10-20 nm in **diam.** + 100-200 nm in **length**). Considerable evidence indicates that PrP 27-30 is required for and inseparable from scrapie infectivity. PrP 27-30 is encoded by a cellular gene and is derived from a larger protein, denoted PrPSc or PrP 33-35Sc, by protease digestion. A cellular isoform, designated PrPC or PprP 33-35C, is encoded by the same gene as PrPSc, and both proteins appear to be translated from the same 2.1 kb mRNA. Monoclonal antibodies to PrP 27-30, as well as antisera to PrP synthetic peptides, specifically react with both PrPC and PrPSc, establishing their relatedness. PrPC is digested by proteinase K, while PrPSc is converted to PrP 27-30 under the same conditions. Prion proteins are synthesized with signal peptides and are integrated into membranes. Detergent extraction of microsomal membranes isolated from scrapie-infected hamster brains solubilizes PrPC but induces PrPSc to polymerize into **amyloid** rods. This procedure allows separation of the two prion protein isoforms and the demonstration that PrPSc accumulates during scrapie infection, while the level of PrPC does not change. The prion **amyloid** rods generated by detergent extraction are identical morphol., except for **length**, to extracellular collections of prion **amyloid** filaments which form plaques in scrapie- and CJD-infected brains. The prion **amyloid** plaques stain with antibodies to PrP 27-30 and PrP peptides. PrP 33-35C does not accumulate in the extracellular space. Prion rods composed of PrP 27-30 can be dissociated into phospholipid vesicles with full retention of scrapie infectivity. The murine PrP gene (Prn-p) is linked to the Prn-i gene which controls the length of the scrapie incubation period. Prolonged incubation times are a cardinal feature of scrapie and CJD. While the central role of PrPSc in scrapie pathogenesis is well established, the chemical as well as conformational differences between PrPC and PrPSc are unknown but probably arise from post-translational modifications.

L58 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on
 STN DUPLICATE 9

ACCESSION NUMBER: 1985:380799 BIOSIS
 DOCUMENT NUMBER: PREV198580050791; BA80:50791
 TITLE: IDENTIFICATION OF PRION **AMYLOID FILAMENTS**
 IN SCRAPIE-INFECTED BRAIN.
 AUTHOR(S): DEARMOND S J [Reprint author]; MCKINLEY M P; BARRY R A;
 BRAUNFELD M B; MCCOLLOCH J R; PRUSINER S B
 CORPORATE SOURCE: DEP OF PATHOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO,
 CALIF 94143, USA
 SOURCE: Cell, (1985) Vol. 41, No. 1, pp. 221-236.
 CODEN: CELLB5. ISSN: 0092-8674.
 DOCUMENT TYPE: Article
 FILE SEGMENT: BA
 LANGUAGE: ENGLISH

AB Extracellular collections of abnormal **filaments** composed of prion proteins were identified in the brains of scrapie-infected hamsters using immunoelectron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted

appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same diameter and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, as determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.